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Maternal Age and Parity in Placenta Praevia

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I. INTRODUCTION.

MULTIPARITY is said to be a powerful predisposing cause of placenta praevia.[1] The frequency of the condition is of the order of 1 per 1,000 labours but it accounts for about 5 per cent of cases of maternal mortality[2] and a still higher percentage of stillbirths.[3] Two types of placenta praevia are distinguished clinically. The placenta may be found to cover the os com-completely (central type): these cases are distinguished from those in which the placental area partly covers the os or has encroached upon the lower uterine segment but has not yet reached beyond the internal os (marginal, lateral, partial or incomplete type*). The two types are said to differ embryologically in that the central type is probably a basal placenta whereas the types which are not central may often be due to capsular extension.[4, 5]

There are some foetal diseases in which it can be easily demonstrated that either multiparity or the age of the mother is a predisposing cause. In most textbooks on children's dis-

* Opinions differ as to what is the correct use of these terms. In this paper "marginal" is taken to mean that the placenta overlaps but does not completely cover the os, and "lateral" is taken to mean that the placental edge does not reach beyond the internal os.

eases, the likelihood of finding that a mongol is last born in a long family is mentioned.[6] Recent investigations have tended to show that there are other conditions, like congenital hydrocephaly and anencephaly, the incidence of which has the same peculiarity.[7, 8] In the case of mongolism, it can be demonstrated that the predisposing factors which depend on maternal age are so important that, in comparison with them, any effect of multiparity is quite insignificant.[9] In the case of other foetal abnormalities, the relative importance of these two factors is not yet known. The association of incidence with maternal age is not confined to abnormalities, for there is strong evidence that the incidence of fraternal twins is affected by maternal age: whether the order of birth of twins has importance as well is not clear from the existing data.

In view of these investigations and of the importance to maternal and foetal health of placenta praevia, it is of interest to investigate statistically the relation of this condition to the two factors of maternal age and maternal parity. A disadvantage, which is inherent in all histories taken at hospital at the time of a patient's being treated, is that the subsequent events cannot be taken into consideration in the analysis of the data. When questions of position in family are studied, this disadvantage is serious. Every obstetric case will be recorded as that of a last-born child. In order to minimize the errors which might creep into the results on account of this peculiarity of hospital records, the investigation of cases of placenta praevia which is described here, was carried out on patients who had been treated in hospital, on the average, 7 years ago. The family history in every case was followed by a personal visit; the number of the mother's pregnancies and the outcome of each were carefully recorded. The data consist of 69 maternal histories, in each of which placenta praevia occurred at least once; in three families it occurred twice.

The cases were treated at Addenbrooke's Hospital, Cambridge, or at the general hospitals in Bury St. Edmunds, Ipswich, or Norwich. By the kindness of the medical staffs of these hospitals the notes were made available for study. The families were all traced and visited by Miss D. A. Newlyn. Miss H. Lang Brown assisted in the arrangement of the data. A summary of each case and the maternal history is given in Appendix I. A subsidiary group of cases (Appendix III) was obtained by Dr. M. Penrose from the records of the Royal Free Hospital, London.

II. Clinical Notes.

In the group of cases on which the main investigation was based there were 38 male children, 29 female children, and 5 whose sexes were not ascertained. It is impossible to infer from these figures whether the sex of the foetus has any significant bearing on the site of the development of the placenta, but the relative excess of males is perhaps worthy of note. Of these 72 children 25 survived, with health apparently unimpaired; in 5 cases the mother died.

Analysis of the information obtained from the hospital records is of some interest in assessing the value of treatment in these cases. Caesarean section was the treatment in 19 cases; in one of these instances the mother died, and in 6 cases the child was stillborn or survived only a few hours. The method of version and delivery after pulling down a leg was applied in 22 cases; in all these the mother survived, but the foetus was stillborn in 19 instances. Other forms of treatment, such as plugging or allowing spontaneous delivery, were less favourable from the point of view of the mother (3 deaths out of 29 cases) and the child died in 20 instances. In two cases the type of treatment could not be ascertained. The figures suggest that Caesarean section is the most satisfactory form of treatment from the point of view of the child and scarcely less favourable than version and extraction from the point of view of the mother. (See Table I.)

Table I.

Survival Rates of Mother and Child in 72 Cases of Placenta Praevia.

Treatment.	Mother.	Child.
Caesarean section	18 out of 19	13 out of 19
Podalic version	22 out of 22	3 out of 22
Other	26 out of 29	9 out of 29
Not specified	1 out of 2	0 out of 2
Total	67 out of 72	25 out of 72

III. Maternal Age.

In order to investigate the significance of maternal age in the aetiology of a given condition, there are two general methods available. One is to compare the maternal ages which corres-

pond to the cases studied with those which correspond to births in the general population.[11] Unfortunately, in this country, statistics are not available which can give the normal maternal age for every pregnancy. Statistics of other countries do not necessarily make a fair comparison, and, in official figures, ages are very often inaccurately recorded. The second method, and the only one available in the present study, is to compare the maternal ages at the affected births with those at the normal births in the same families. This comparison gives exact information only in so far as the families are complete. On the other hand, if we wish merely to ask whether maternal age or birth rank (parity) is likely to be the more important aetiological factor, then the fact that a few of the families may not be complete is of no consequence. Furthermore, the ages at affected births cannot be fairly compared with the ages at normal births unless allowance is made for size of family. In any investigation in which families are picked by the presence of at least one affected member, the mean number of brothers and sisters tends to be too large as compared with the mean number in the general community.[12]

The method of comparison used here was first to allot an appropriate expectation to each pregnancy. Thus, if a family is found to contain three normal births and one case of placenta praevia, the random chance—that is, expectation—of the occurrence of placenta praevia at each of the four pregnancies is one quarter. For purposes of attributing these expectations, miscarriages were excluded. After allotting the expectations in each family, the total expectation was added up for each year of maternal age: the result of this calculation is given in Table II where the expected and observed numbers of cases of placenta praevia at each maternal age are recorded. The expected mean maternal age at normal births is seen to be 29.10 years; the observed mean maternal age of all the cases of placenta praevia is 31.86 years. The difference between these two means is therefore 2.76, and this is a highly significant value in the statistical sense: it is nearly four times the standard error, which is ±0.71 years. From this calculation there is a good prima facie case for believing that maternal age is a factor of significance in the aetiology of placenta praevia. The effect might be slightly lessened had all the families in the data been finished.

TABLE II.

72 Cases of Placenta Praevia.

Maternal age in years.	Number observed.	Number expected.
16	—	0.06
17	—	—
18	—	0.75
19	1	1.15
20	1	1.82
21	2	2.75
22	2	3.55
23	5	6.44
24	4	3.78
25	—	2.41
26	6	4.76
27	—	4.38
28	5	4.03
29	3	3.32
30	2	3.29
31	1	2.74
32	6	4.46
33	4	3.49
34	3	3.74
35	2	3.08
36	5	4.05
37	2	1.75
38	2	0.70
39	5	1.23
40	2	0.94
41	3	1.95
42	3	0.67
43	—	0.33
44	2	0.14
45	—	—
46	1	0.09
Total	72	71.85
Mean	31.86	29.10
Standard deviation (σ_A) ...	—	5.99
Standard error ($\sigma_A \sqrt{72}$)	—	0.71

IV. Maternal Parity.

The comparison between expected and observed numbers of cases of placenta praevia in each birth rank is shown in Table III. There is evidently a tendency for mothers with a high degree of multiparity to be represented in the series. There is also no obvious tendency for the condition to affect the first born.

Table III.

72 Cases of Placenta Praevia.

Birth rank.	Number observed.	Number expected.
1st	20	27.65
2nd	14	18.82
3rd	15	10.93
4th	6	4.98
5th	4	3.23
6th	2	1.76
7th	3	1.52
8th	4	0.93
9th	—	0.58
10th	—	0.44
11th	1	0.34
12th	1	0.23
13th	1	0.14
14th	—	—
15th	—	0.06
16th	—	0.12
17th	—	0.06
18th	1	0.06
Total	72	71.85
Mean	3.55	2.58
Standard deviation (σ_R) ...	—	2.20
Standard error ($\sigma_R\sqrt{72}$)	—	0.26

The mean rank of all cases was not as high as might have been guessed from inspection of the data: the average number of previous pregnancies was only between two and three—that is to say, the mean birth rank for placenta praevia was 3.55. This value was higher than that of expected normal births, namely 2.58. The difference of almost one rank between

observed and expected values is statistically significant and is nearly as significant as the maternal age difference shown in Table II.

V. Relative Importance of Age and Parity.

From Tables II and III it appears likely that maternal age and multiparity are almost equally important aetiological factors in the causation of placenta praevia, but the point needs further analysis. There is more than one method by which the separation of aetiological importance of age and rank may be attempted. The most accurate method is that which was used elsewhere[13] to find out whether birth rank could have any significance in the aetiology of mongolism. This method is very laborious, and it is not reasonable to attempt it unless there is a fair likelihood that a definite result will be obtained. In the present limited amount of data, the significance of a result obtained by that method might still be in doubt. We can, however, analyse the present data by a much simpler method which, though less exact, may give suggestive results. This method involves finding out the correlation between expected age and expected rank in all the families and, for this purpose, a detailed table of expectations had to be prepared: in Table IV the ranks and ages have been grouped in order to save space. The degree of correlation of the expectations for age and rank was found to be +0.454. This calculation allows regression equations of the ordinary kind[14] to be calculated and the mean expected maternal age for placenta praevia, on the assumption that rank is of no significance, can then be discovered. This expected mean maternal age, which is actually 30.3 years,* with a standard error of ±0.63 years, is still significantly lower than the mean observed age (31.86 years).

The converse comparison can be made by obtaining expected ranks based on constant maternal age from the regression equations; that is to say, to study the effect of birth rank, or parity, by itself, we eliminate the effect of maternal age. The expected birth rank (3.04)† is still found to be below the observed value (3.55) and again the difference (0.51±0.23) is just significant. Probably, therefore, multiparity has its independent effect, though this may be less important than the effect of maternal age.

* $\sigma_A/\sigma_R(0.454)(3.55-2.58)+29.10=30.30$.

† $\sigma_R/\sigma_A(0.454)(31.86-29.10)+2.58=3.04$.

TABLE IV.

72 Cases of Placenta Praevia classified according to Birth Order and Maternal Age, with Expectations.

Maternal age in years.	Birth rank. 1	2–3	4–6	7–10	11–15	16–18	TOTAL
16–19	*1*	—	—	—	—	—	*1*
	1.57	0.39	—	—	—	—	1.96
20–24	*8*	*5*	*1*	—	—	—	*14*
	9.88	7.91	0.55	—	—	—	18.34
25–29	*3*	*7*	*4*	—	—	—	*14*
	6.04	9.13	3.53	0.20	—	—	18.90
30–34	*6*	*9*	*1*	—	—	—	*16*
	7.33	6.75	3.11	0.41	0.12	—	17.72
35–39	*1*	*7*	*3*	*5*	—	—	*16*
	1.83	5.07	2.06	1.65	0.20	—	10.81
40–44	*1*	*1*	*3*	*2*	*2*	*1*	*10*
	1.00	0.50	0.72	1.21	0.36	0.24	4.03
45–49	—	—	—	—	*1*	—	*1*
	—	—	—	—	0.09	—	0.09
TOTAL	*20*	*29*	*12*	*7*	*3*	*1*	*72*
	27.65	29.75	9.97	3.47	0.77	0.24	71.85

VI. CENTRAL CASES COMPARED WITH OTHERS.

The 72 cases in the present survey could be separated into three groups: those definitely described as central (21 cases), those described as marginal or lateral (39 cases), and a few in which the type was unspecified (12 cases). The mean number of pregnancies was almost exactly the same in both central and non-central groups, but the mean maternal age was greater for the central cases. (See Table V.) Calculation of the most likely maternal age which corresponds to this mean number of pregnancies reveals that, even with such a small number of cases the maternal age for central placenta praevia is significantly

TABLE V.

Source of material.	Central Placenta Praevia. No. of cases.	Average maternal age in years.	Aver. birth rank.	Marginal or Lateral Placenta Praevia No. of cases.	Average maternal age in years.	Aver. birth rank.
Present series	21	33.71	3.48	... 39	31.21	3.46
Palmer[15]	3	31.00	1.67	... 8	32.25	4.12
Royal Free Hospital ...	11	34.73	2.09	... 65	31.46	3.68
Total	35	33.80	2.89	... 112	31.43	3.63

All Clinical Types of Placenta Praevia
(12 *cases of unspecified type included.*)

Number of cases.	Mean maternal age in years.	Mean birth rank.
159	31.90	4.04

These figures can be compared with the mean maternal age of 32.04 years in 3,602 cases of placenta praevia and the mean birth rate of 4.04 in 4,406 cases. (See C. Berkeley, "Unavoidable Haemorrhage," *Journ. Obstet. and Gynaecol. Brit. Emp.*, 1936, xliii, 393.)

high. On the other hand, the mean maternal age for the marginal and lateral cases is not abnormally high if the birth rank is taken into consideration.

This distinction between central cases and other types is emphasized by comparison of data from the present survey with data derived from other sources. Even in the small group of cases, described by Palmer[15] (Appendix II), for example, if allowance is made for the difference in degree of parity, the mothers in the three central cases are relatively older than the mothers in the eight non-central cases. In the material collected from the Royal Free Hospital case-notes, which is much more extensive, an even more marked distinction is shown. All data from the three sources are combined in Table V. The average maternal age for 35 cases is more than two years greater than that for 112 marginal and lateral cases although the mean number of pregnancies is less in the central cases than in the others.

On purely statistical grounds it appears likely that, between the two sorts of cases which are clinically distinguished, there lies a real aetiological difference. The observed mean birth rank for central cases is consistent with the view that, in comparison with increased maternal age, parity is of no aetiological importance. In the group of cases classified as marginal or lateral it is not possible to distinguish whether age or parity has the greater effect. Indeed, there may be included in this group some which are aetiologically related to the central type and others in which the number of pregnancies is the main determining factor. Further information on this point was not obtained, however, by the separation of these cases into two classes —those diagnosed as marginal and those diagnosed as lateral type.

Closely associated with the question of the significance of multiparity is the possibility that too short an interval between pregnancies may act as a predisposing cause in placenta praevia. Inspection of the present data, however, reveals that the interval between the abnormal pregnancy and that immediately preceding it is not unduly short in comparison with other pregnancy intervals in the families studied.

It is sometimes believed that central placenta praevia has a preference for first pregnancies but that this is not the case with the marginal type. Of the central cases mentioned in Table V, 12 out of 35, or 34 per cent, were in primparae, and only 26 out of 112, of 23 per cent, of the marginal or lateral cases were in primiparae. The greater likelihood of primiparous central cases may be due to the fact that the families are close to normal size in these cases because here multiparity does not appear to be a predisposing cause.

VII. Summary.

An investigation into the maternal histories of 72 cases of placenta praevia has been described. The material collected, together with some additional data, has been analysed in such a manner as to obtain information about the aetiological importance of maternal age and multiparity. The results suggest that increasing maternal age is a significant factor in producing the central type, though multiparity can be the chief cause in some marginal and lateral cases.

I am much indebted to Professor A. Fleming for permitting access to the notes of her cases and allowing the results to be

made use of in this paper. The work has been carried through under the auspices of the Medical Research Council and the Darwin Trust, in association with parallel inquiries into the effects of birth order and maternal age on the incidence of various abnormalities.

I am grateful to Mr. Eardley Holland for his advice and encouragement.

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APPENDIX I.

Summary of the Histories in 72 Cases of Placenta Praevia 69 Families

The pregnancies are arranged in order of birth.

* indicates the affected pregnancy in each case.

The age given is that of the mother at the time of each birth.

The figures in brackets show the expectation of placenta praevia allotted to each pregnancy except those resulting in miscarriages.

No. 1.

Mother. Now aged 42: has a contracted pelvis.

Pregnancies.

1st at age 35: forceps delivery of female child who died at 12 days. (0.33).

2nd at age 36: induced labour at thirty-second week; healthy female child. (0.33).

*3rd at age 38: central placenta praevia; Caesarean section and salpingectomy; healthy male child. (0.33).

No. 2.

Mother. Now aged 36.

Pregnancies.

*1st at age 33: central placenta praevia; Caesarean section; female child lived 31 hours. (0.50).

2nd at age 35: Caesarean section for obstructed labour; normal placenta; healthy female child. (0.50).

No. 3.

Mother. Now aged 38.

Pregnancies.

1st at age 27: normal birth of healthy female child. (0.25).

*2nd at age 32: marginal placental praevia; podalic version and extraction of stillborn female child. (0.25).

3rd at age 35: normal birth of healthy male child. (0.25).

4th at age 37: normal birth of healthy female child. (0.25).

No. 4.

Mother. Now aged 45.

Pregnancies.

1st at age 27: stillborn female child. (0.33).

2nd at age 28: normal birth of healthy female child. (0.33).

*3rd at age 32: placenta praevia; Caesarean section; healthy male child. (0.33).

No. 5.

Mother. Now aged 35: states that she had some haemorrhage after the birth of second child and had bleeding for the first two months of fourth pregnancy.

Pregnancies.

1st at age 21: normal birth of healthy male child. (0.20).
2nd at age 22: normal birth of healthy female child. (0.20).
3rd at age 24: normal birth of healthy male child. (0.20).
4th at age 27: normal birth of healthy male child. (0.20).
*5th at age 29: marginal placenta praevia; spontaneous vertex delivery of healthy female child who died of pneumonia at 1 year 2 months. (0.20).
6th at age 34: miscarriage at 2½ months.

No. 6.

Mother. Now aged 38.

Pregnancies.

1st at age 25: forceps delivery of healthy male child. (0.33).
*2nd at age 32: lateral placenta praevia; vertex delivery by Willett's forceps of female child who lived 50 minutes. (0.33).
3rd at age 37: forceps delivery of healthy female child. (0.33).

No. 7.

Mother. Now aged 38.

Pregnancies.

*1st at age 31: central placenta praevia; podalic version and extraction; spontaneous delivery of stillborn male child. (1.00).

No. 8.

Mother. Now aged 48.

Pregnancies.

1st at age 29: normal birth of healthy female child who died at 2 years of diphtheria. (0.25).
2nd at age 32: normal birth of healthy male child. (0.25).
3rd at age 34: normal birth of healthy female child. (0.25).
*4th at age 39: central pracenta praevia; podalic version and extraction of stillborn male child. (0.25).

No. 9.

Mother. Now aged 40.

Pregnancies.

*1st at age 30: marginal placenta praevia; podalic version and extraction of healthy male child. (1.00).

No. 10.

Mother. Now aged 41:

Pregnancies.

*1st at age 28: placenta praevia; spontaneous delivery of anencephalic child of unknown sex. (0.50).

2nd at age 35: normal birth of healthy female child. (0.50).

No. 11.

Mother. Died 12 years ago at the age of 28.

Pregnancies.

*1st at age 28: central placenta praevia; treatment—pituitrin; patient died; child unborn. (1.00).

No. 12.

Mother. Now aged 44.

Pregnancies.

1st at age 29: normal birth of healthy male child. (0.33).

2nd at age 30: normal birth of healthy male child. (0.33).

*3rd at age 35: placenta praevia; Caesarean section; healthy male child. (0.33).

No. 13.

Mother. Now aged 45.

Pregnancies.

1st at age 27: forceps delivery of healthy male child. (0.50).

*2nd at age 36: marginal placenta praevia; spontaneous delivery of healthy female child. (0.50).

No. 14.

Mother. Now aged 37.

Pregnancies.

1st at age 24: normal birth of healthy male child. (0.33).

2nd at age 28: normal birth of stillborn female child. (0.33).

*3rd at age 30: marginal placenta praevia; podalic version and extraction of stillborn female child. (0.33).

No. 15.

Mother. Now aged 29.

Pregnancies.

*1st at age 24: marginal placenta praevia; podalic version; healthy male child. (1.00).

No. 16.

Mother. Now aged 34.

Pregnancies.

1st at age 20: normal birth of healthy male child. (0.25).

2nd at age 24: normal birth of healthy male child. (0.25).

*3rd at age 26: marginal placenta praevia; podalic version and extraction of healthy male child. (0.25).
4th at age 32: normal birth of healthy female child. (0.25).

No. 17.

Mother. Now aged 35.
Pregnancies.
1st at age 22: normal birth of healthy male child. (0.50).
*2nd at age 23: central placenta praevia; podalic version and extraction of stillborn child. (0.50).

No. 18.

Mother. Now aged 42.
Pregnancies.
1st at age 31: normal birth of healthy female child. (0.50).
*2nd at age 33: lateral placenta praevia; podalic version and extraction of stillborn female child. (0.50).

No. 19.

Mother. Now aged 36.
Pregnancies.
1st at age 22: normal birth of healthy female child. (0.33).
2nd at age 25: normal birth of healthy male child. (0.33).
*3rd at age 28: placenta praevia; Caesarean section; healthy female child. (0.33).

No. 20.

Mother. Now aged 27.
Pregnancies.
1st at age 20: normal birth of healthy male child. (0.33).
2nd at age 22: normal birth of healthy female child. (0.33).
*3rd at age 23: central placenta praevia; podalic version; stillborn male child. (0.33).

No. 21.

Mother. Now aged 24.
Pregnancies.
*1st at age 21: marginal placenta praevia: spontaneous vertex delivery of healthy male child. (0.33).
2nd at age 22: normal birth of healthy female child. (0.33).
3rd at age 23: normal birth of healthy female child. (0.33).

No. 22.

Mother. Now aged 43.
Pregnancies.
1st at age 20: twin birth of healthy male children. (0.50).
2nd at age 23: forceps delivery of male child who had fits and died at 5 months. (0.25).

*3rd at age 32: central placenta praevia; Caesarean section; stillborn male child. (0.25).

No. 23.

Mother. Now aged 31.

Pregnancies.

1st at age 21: normal birth of healthy male child. (0.20).
2nd at age 22: normal birth of healthy female child. (0.20).
3rd at age 23: difficult birth, on account of short cord, of healthy male child. (0.20).
4th at age 25: normal birth of healthy male child. (0.20).
*5th at age 28: marginal placenta praevia; podalic version and extraction of stillborn male child. (0.20).

No. 24.

Mother. Now aged 43; had two healthy male children by previous marriage.

Pregnancies.

3rd at age 31: normal birth of healthy female child. (0.11).
4th at age 33: normal birth of healthy male child. (0.11).
5th at age 34: normal birth of healthy male child. (0.11).
6th at age 36: normal birth of healthy female child. (0.11).
7th at age 37: normal birth of healthy male child. (0.11).
8th at age 39: normal birth of healthy male child. (0.11).
9th at age 40: normal birth of healthy female child. (0.11).
10th at age 41: slight antepartum haemorrhage; premature birth of male child who lived 3 days. (0.11).
*11th at age 42: placenta praevia (not central); spontaneous delivery of stillborn female child. (0.11).

No. 25.

Mother. Now aged 47.

Pregnancies.

1st at age 21: forceps delivery of healthy female child. (0.17).
2nd at age 22: normal birth of healthy female child. (0.17).
3rd at age 23: normal birth of healthy male child. (0.17).
4th at age 26: normal birth of healthy male child. (0.17).
5th at age 29: normal birth of healthy male child. (0.17).
6th at age 34: miscarriage at 3½ months.
*7th at age 40: lateral placenta praevia; forceps delivery of stillborn female child. (0.17).

No. 26.

Mother. Now aged 41.

Pregnancies.

1st at age 30: forceps delivery of healthy female child. (0.50).
*2nd at age 36: central placenta praevia; podalic version; stillborn male child. (0.50).

No. 27.

Mother. Now aged 33.

Pregnancies.

1st at age 23: normal birth of female child who died at 1 year 3 months of meningitis. (0.25).

2nd at age 25: normal birth of healthy male child. (0.25).

*3rd at age 26: placenta praevia; Caesarean section; healthy female child. (0.25).

4th at age 29: normal birth of healthy female child. (0.25).

No. 28.

Mother. Now aged 47.

Pregnancies.

1st at age 27: normal birth of healthy male child. (0.50).

*2nd at age 35: placenta praevia (not central); podalic version; spontaneous delivery of healthy male child. (0.50).

No. 29.

Mother. Now aged 33.

Pregnancies.

*1st at age 24: central placenta praevia; podalic version and extraction of stillborn female child, 12 weeks premature. (0.50).

2nd at age 27: normal birth of healthy female child. (0.50).

No. 30.

Mother. Now aged 46.

Pregnancies.

1st at age 18: normal birth of healthy female child. (0.14).

2nd at age 21: normal birth of healthy male child. (0.14).

3rd at age 23: normal birth of healthy male child. (0.14).

4th at age 26: normal birth of female child with congenital heart lesion who died at 5 weeks. (0.14).

5th at age 31: normal birth of healthy female child. (0.14).

6th at age 36: normal birth of healthy male child. (0.14).

*7th at age 42: placenta praevia (not central); Caesarean section; healthy female child. (0.14).

No. 31.

Mother. Now aged 48.

Pregnancies.

1st at age 23: normal birth of healthy male child. (0.14).

2nd at age 28: normal birth of weakly female child, who died at 18 years of pneumonia. (0.14).

3rd at age 30: normal birth of healthy male child. (0.14).

4th at age 34: normal birth of healthy male child. (0.14).

5th at age 35: normal birth of healthy male child. (0.14).

*6th at age 41: placenta praevia (not central); podalic version; manual removal of adherent placenta; stillborn male child. (0.14).
7th at age 43: normal birth of weakly male child. (0.14).

No. 32.

Mother. Now aged 35.
Pregnancies.
1st at age 22: forceps delivery of healthy female child. 0.33).
2nd at age 23: breech delivery of healthy male child. (0.33).
*3rd at age 24: placenta praevia (not central); spontaneous delivery, but adherent placenta, of male child who lived 2 hours. (0.33).
*4th at age 26: placenta praevia; Caesarean section; healthy male child. (0.33).
5th at age 30: forceps delivery of healthy female child. (0.33).
6th at age 32: forceps delivery of healthy male child. (0.33).

No. 33.

Mother. Died 9 years ago at the age of 41 of exophthalmic goitre of 11 years' duration.
Pregnancies.
1st at age 30: transverse presentation of male child who died immediately after birth. (0.25).
2nd at age 31: miscarriage at 5½ months.
3rd at age 33: malpresentation of stillborn male child. (0.25).
4th at age 35: malpresentation of healthy male child. (0.25).
*5th at age 39: placenta praevia (not central); shoulder presentation; treatment not recorded; stillborn male child. (0.25).

No. 34.

Mother. Now aged 32.
Pregnancies.
*1st at age 24: marginal placenta praevia; podalic version and extraction of stillborn male child. (0.33).
2nd at age 27: normal birth of healthy male child. (0.33).
3rd at age 28: normal birth of healthy male child. (0.33).

No. 35.

Mother. Now aged 24.
Pregnancies.
1st at age 18: normal birth of male child who died at 10 weeks of pneumonia. (0.33).
2nd at age 19: forceps delivery of healthy male child. (0.33).
3rd at age 20: miscarriage.
*4th at age 20: marginal placenta praevia; rupture of membranes; healthy male child. (0.33).

No. 36.

Mother. Now aged 26.

Pregnancies.

1st at age 22: miscarriage.

*2nd at age 23: marginal placenta praevia; podalic version and extraction of stillborn male child. (0.50).

3rd at age 25: normal birth of healthy male child. (0.50).

No. 37.

Mother. Now aged 29.

Pregnancies.

*1st at age 21: marginal placenta praevia; breech presentation of stillborn male child. (0.33).

2nd at age 23: normal birth of healthy female child. (0.33).

3rd at age 26: normal birth of healthy male child. (0.33).

No. 38.

Mother. Now aged 34.

Pregnancies.

*1st at age 23: marginal placental praevia; spontaneous delivery of healthy female child. (0.20).

2nd at age 25: normal birth of healthy female child. (0.20).

3rd at age 26: normal birth of healthy female child. (0.20).

4th at age 27: normal birth of healthy female child. (0.20).

5th at age 31: normal birth of healthy male child. (0.20).

No. 39.

Mother. Now aged 43.

Pregnancies.

1st at age 24: forceps delivery of healthy male child. (0.13).

2nd at age 25: normal birth of healthy female child. (0.13).

3rd at age 27: normal birth of healthy female child. (0.13).

4th at age 29: normal birth of healthy female child. (0.13).

5th at age 31: forceps delivery of healthy male child. (0.13).

6th at age 33: normal birth of healthy male child. (0.13).

7th at age 35: normal birth of healthy female child. (0.13).

*8th at age 39: marginal placenta praevia; spontaneous delivery of healthy male child. (0.13).

No. 40.

Mother. Now aged 36.

Pregnancies.

1st at age 26: normal birth of healthy male child. (0.33).

2nd at age 32: normal birth of healthy female child. (0.33).

*3rd at age 33: placenta praevia (not central); spontaneous delivery of stillborn male child. (0.33).

No. 41.

Mother. Now aged 40.

Pregnancies.

1st at age 27: normal birth of healthy female child. (0.50).

*2nd at age 37: marginal placenta praevia; delivery, by Willett's forceps, of healthy female child. (0.50).

No. 42.

Mother. Died 2 years ago at the age of 29.

Pregnancies.

1st at age 26: normal birth of male child with spina bifida who lived 2 days. (0.50).

*2nd at age 29: central placenta praevia; no record of the treatment; stillborn female child. (0.50).

No. 43.

Mother. Died 7 years ago, at the age of 22, of peritonitis.

Pregnancies.

1st at age 20: normal birth of healthy female child. (0.33).

2nd at age 21: normal birth of healthy female child. (0.33).

*3rd at age 22: marginal placenta praevia; Caesarean section; healthy male child. (0.33).

No. 44.

Mother. Died 8 years ago at the age of 41.

Pregnancies.

*1st at age 41: central placenta praevia; plugging; child unborn. (1.00).

No. 45.

Mother. Died 5 years ago at the age of 33.

Pregnancies.

*1st at age 26: placenta praevia; podalic version and spontaneous delivery of stillborn male child. (0.33).

2nd at age 28: premature stillborn female child. (0.33).

3rd at age 33: premature stillborn male child. (0.33).

No. 46.

Mother. Now aged 55.

Pregnancies.

1st at age 18: normal birth of healthy male child. (0.08).

2nd at age 20: normal birth of healthy female child. (0.08).

3rd at age 21: normal birth of healthy female child. (0.08).

4th at age 23: normal birth of healthy female child. (0.08).

5th at age 23: normal birth of healthy male child.(0.08).

6th at age 28: normal birth of female child who died of measles at 1 year 5 months. (0.08).

7th at age 29: normal birth of healthy male child. (0.08).

8th at age 30: normal birth of healthy female child. (0.08).
9th at age 32: normal birth of healthy male child. (0.08).
10th at age 36: normal birth of healthy female child. (0.08).
11th at age 38: normal birth of healthy male child. (0.08).
12th at age 40: normal birth of healthy female child. (0.08).
*13th at age 44: central placenta praevia; version and extraction of stillborn male child. (0.08).

No. 47.

Mother. Now aged 41.
Pregnancies.
1st at age 19: normal birth of healthy male child. (0.17).
2nd at age 23: normal birth of healthy male child. (0.17).
3rd at age 25: normal birth of healthy male child. (0.17).
4th at age 27: normal birth of healthy male child. (0.17).
5th at age 28: normal birth of healthy male child. (0.17).
*6th at age 32: placenta praevia; Caesarean section; healthy male child. (0.17).
7th at age 38: miscarriage at 3 months.

No. 48.

Mother. Now aged 58.
Pregnancies.
1st at age 19: normal birth of healthy male child. (0.09).
2nd at age 23: normal birth of healthy male child. (0.09).
3rd at age 26: normal birth of female child who died of diphtheria at 10 years. (0.09).
4th at age 28: normal birth of healthy male child. (0.09).
5th at age 30: miscarriage at 3 months.
6th at age 31: miscarriage at 6 months.
7th at age 33: normal birth of healthy male child. (0.09).
8th at age 35: normal birth of healthy male child. (0.09).
9th at age 38: twin birth of stillborn male child and female child who lived 22 hours. (0.18).
10th at age 42: normal birth of healthy male child. (0.09).
11th at age 43: premature birth of female child who lived 12 hours. (0.09).
*12th at age 46: central placenta praevia; placenta was in two pieces, joined by a membrane: one piece covered the internal os; Caesarean section; male child, who died of scarlet fever at 5 years. (0.09).

No. 49.

Mother. Now aged 42.
Pregnancies.
1st at age 36: forceps delivery of male hydrocephalic imbecile, who died at 11 months. (0.50).

*2nd at age 41: placenta praevia; Caesarean section; stillborn female child. (0.50).

No. 50.

Mother. Now aged 46.

Pregnancies.

*1st at age 36: marginal placenta praevia; breech delivery of stillborn female child, 12 weeks premature. (1.00).

No. 51.

Mother. Now aged 29.

Pregnancies.

*1st at age 23: marginal placenta praevia; breech delivery of healthy female child. (1.00).

*2nd at age 26: marginal placenta praevia; delivery by Willett's forceps of stillborn male child. (1.00).

No. 52.

Mother. Now aged 41.

Pregnancies.

1st at age 21: normal birth of healthy female child. (0.11).

2nd at age 23: normal birth of healthy female child. (0.11).

3rd at age 27: normal birth of healthy female child. (0.11).

4th at age 29: normal birth of female child, who died of pneumonia at 1 year 6 months. (0.11).

5th at age 31: forceps delivery of healthy female child, whose right arm was injured at birth. (0.11).

6th at age 34: normal birth of healthy male child. (0.11).

7th at age 37: normal birth of healthy female child. (0.11).

*8th at age 38: central placenta praevia; spontaneous delivery with placenta of stillborn female child. (0.11).

9th at age 40: normal birth of healthy female child. (0.11).

No. 53.

Mother. Now aged 44; has a small pelvis.

Pregnancies.

1st at age 30: breech delivery of male child who lived 3 days. (0.33).

2nd at age 32: Caesarean section; healthy male child. (0.33).

*3rd at age 34: marginal placenta praevia; spontaneous delivery of stillborn female child. (0.33).

4th at age 38: miscarriage at 1 month.

No. 54.

Mother. Now aged 30.

Pregnancies.

1st at age 23: normal birth of healthy male child. (0.33).

*2nd at age 26: central placenta praevia; Caesarean section; male child, with diaphragmatic hernia and transposition of great vessels, lived 45 minutes. (0.33).
3rd at age 29: normal birth of healthy female child. (0.33).

No. 55.

Mother. Now aged 43.
Pregnancies.
1st at age 31: premature birth of stillborn female child. (0.25).
2nd at age 32: premature birth of healthy female child. (0.25).
3rd at age 33: miscarriage at 2 months.
4th at age 33: premature birth of stillborn male child with hare-lip and other deformities. (0.25).
5th at age 34: premature twin birth of 1 healthy female child and 1 stillborn female child. (0.50).
6th at age 36: normal birth of healthy male child. (0.25).
*7th at age 37: placenta praevia (not central); female child lived 24 hours. (0.25).
*8th at age 39: placenta praevia (not central); stillborn female child. (0.25).

No. 56.

Mother. Now aged 47; bleeding during 5th month of 4th pregnancy.
Pregnancies.
1st at age 16: normal birth of healthy female child. (0.06).
2nd at age 19: normal birth of healthy male child. (0.06).
3rd at age 21: normal birth of healthy male child. (0.06).
4th at age 23: normal birth of healthy female child. (0.06).
5th at age 25: normal birth of healthy female child. (0.06).
6th at age 26: normal birth of male child who died at 1 year 2 months. (0.06).
7th at age 27: membranes ruptured 2 weeks before delivery of healthy female child. (0.06).
8th at age 29: normal birth of healthy male child. (0.06).
9th at age 30: miscarriage at 4½ months.
10th at age 31: normal birth of healthy female child. (0.06).
11th at age 32: normal birth of healthy male child. (0.06).
12th at age 34: premature birth of healthy male child. (0.06).
13th at age 35: normal birth of healthy female child. (0.06).
14th at age 36: miscarriage.
15th at age 37: normal birth of healthy female child. (0.06).
16th at age 40: twin birth of healthy male child and male child who lived lived 3 days. (0.06).
17th at age 41: normal birth of healthy male child. (0.06).
*18th at age 44: placenta praevia; podalic version and extraction of stillborn female child. (0.06).

No. 57.

Mother. Now aged 22.

Pregnancies.

*1st at age 19: marginal placenta praevia; Caesarean section; healthy female child. (0.50).

2nd at age 21: normal birth of healthy male child. (0.50).

No. 58.

Mother. Now aged 38.

Pregnancies.

*1st at age 34: marginal placenta praevia; delivery by Willett's forceps of healthy male cihld. (1.00).

No. 59.

Mother. Died 7 years ago at the age of 33.

Pregnancies.

1st at age 23: normal birth of healthy female child. (0.50).

*2nd at age 33: central placenta praevia; plugging; child unborn. (0.50).

No. 60.

Mother. Now aged 43.

Pregnancies.

*1st at age 32: central placenta praevia; Caesarean section; healthy female child. (1.00).

No. 61.

Mother. Now aged 44; had some haemorrhage during first 2 months of 9th pregnancy.

Pregnancies.

1st at age 21: normal birth of healthy male child. (0.10).

2nd at age 23: normal birth of healthy male child. (0.10).

3rd at age 24: normal birth of healthy male child. (0.10).

4th at age 25: normal birth of healthy male child. (0.10).

5th at age 27: normal birth of healthy male child. (0.10).

6th at age 31: normal birth of healthy male child. (0.10).

7th at age 34: occipito-posterior presentation of healthy female child. (0.10).

*8th at age 39: marginal placenta praevia; treatment, pituitrin; breech delivery of stillborn male child. (0.10).

9th at age 40: normal birth of healthy male child. (0.10).

10th at age 43: normal birth of healthy male child. (0.10).

No. 62.

Mother. Now aged 49.

Pregnancies.

1st at age 25: normal birth of healthy male child. (0.14).

2nd at age 31: normal birth of healthy male child. (0.14).

3rd at age 34: normal birth of healthy male child. (0.14).
*4th at age 36: central placenta praevia; podalic version and extraction of stillborn female child. (0.14).
5th at age 37: normal birth of healthy female child. (0.14).
6th at age 39: normal birth of healthy female child. (0.14).
7th at age 41: normal birth of healthy male child. (0.14).

No. 63.

Mother. Now aged 40.
Pregnancies.
*1st at age 34: marginal placenta praevia; membranes ruptured; delivery by Willett's forceps of stillborn male child. (1.00).

No. 64.

Mother. Now aged 31.
Pregnancies.
*1st at age 22: placenta praevia; Caesarean section; stillborn male child. (0.50).
2nd at age 27: normal birth of healthy male child. (0.50).

No. 65.

Mother. Now aged 43.
Pregnancies.
1st at age 26: normal birth of healthy male child. (0.25).
2nd at age 29: normal birth of healthy female child. (0.25).
3rd at age 32: normal birth of healthy male child. (0.25).
*4th at age 40: central placenta praevia; Caesarean section; healthy female child. (0.25).

No. 66.

Mother. Now aged 51.
Pregnancies.
1st at age 23: forceps delivery of healthy male child. (0.33).
2nd at age 26: miscarriage.
3rd at age 29: normal birth of healthy male child. (0.33).
*4th at age 42: marginal placenta praevia with 2 lobes; treatment, pituitrin; forceps, vertex delivery of stillborn male child. (0.33).

No. 67.

Mother. Now aged 38.
Pregnancies.
1st at age 22: normal birth of healthy male child. (0.33).
2nd at age 24: normal birth of stillborn male child. (0.33).
*3rd at age 29: placenta praevia; Caesarean section; stillborn female child. (0.33).

No. 68.

Mother. Now aged 31; at each parturition the placenta was slow in separating.

Pregnancies.

1st at age 18: normal birth of healthy female child. (0.20).
2nd at age 21: normal birth of healthy male child. (0.20).
3rd at age 24: normal birth of healthy male child. (0.20).
4th at age 26: normal birth of healthy female child. (0.20).
*5th at age 28: lateral placenta praevia; prolapsed cord; spontaneous breech delivery; manual removal of placenta; stillborn male child. (0.20).

No. 69.

Mother. Now aged 44.

Pregnancies.

1st at age 31: miscarriage at 4½ months.
2nd at age 33: normal birth of healthy female child. (0.50).
*3rd at age 36: central placenta praevia; podalic version and extraction of stillborn male child. (0.50).

APPENDIX II.

CASES OF PLACENTA PRAEVIA DESCRIBED BY PALMER (*Med. Res. Coun. Sp. Rep.*, Series No. 118, 1928).

Central			*Not Central*		
Reference number	Maternal age	Pregnancy number	Reference number	Maternal age	Pregnancy number
lviii	28	3	xlviii	36	3
lxx	33	1	xlix	38	9
cxxxv	32	1	liii	31	1
			lxviii	39	6
			lxix	20	1
			xci	42	5
			xcviii	24	3
			cxxxvi	28	5

APPENDIX III.

CASES OF PLACENTA PRAEVIA TREATED IN THE ROYAL FREE HOSPITAL, 1928 TO 1938.

Date	*Central* Patient's initials	Maternal age	Pregnancy number
1928	D.B.	34	3
1929	K.P.	27	2
1932	E.C.	41	3
1933	M.B.	32	1
1934	I.M	41	2
1934	A.D.	34	1
1935	R.B.	28	2
1936	F.B.	31	3
1937	F.M.	40	4
1937	J.J.	32	1
1938	F.C.	42	1

Not Central							
Marginal				*Lateral*			
Date	Patient's initials	Maternal age	Pregnancy number	Date	Patient's initials	Maternal age	Pregnancy number
1929	M.M.	33	3	1930	K.W.	26	4
1929	E.D.	39	4	1930	M.S.	24	2
1930	N.D.	37	3	1930	N.R.	29	2
1930	W.B.	29	1	1930	K.R.	39	10
1930	C.S.	25	5	1930	E.N.	38	3
1931	L.M.	31	2	1930	M.J.	33	1
1931	G.E.	28	1	1930	E.H.	24	1
1931	A.B.	35	6	1930	L.C.	25	2
1932	E.W.*	37	11	1930	V.C.	31	5
1932	R.S.	29	3	1930	F.B.	27	2
1932	M.B.	39	8	1931	K.W.	23	2
1932	E.B.	36	3	1931	S.T.	40	6
1933	S.I..	38	8	1931	E.H.	45	8
1933	A.C.	20	1	1931	E.C.	24	1
1933	B.B.	27	2	1931	W.B.	22	1
1933	C.S.	28	4	1931	D.F.†	32	1
1933	M.H.	26	2	1932	E.S.	19	1
1933	A.D.	38	9	1932	A.B.	37	2
1934	G.L.	26	1	1933	E.W.*	38	12
1934	L.S.	35	4	1933	D.F.†	34	2
1935	R.S.	43	3	1934	V.V.	35	4
1935	L.G.	26	1	1934	M.K.	42	11
1935	J.P.	36	9	1936	J.B.	24	3
1935	E.S.	34	2	1936	E.H.	26	2
1936	I.B.	28	1	1936	L.B.	31	2
1937	R.J.	25	2	1936	C.M.	43	9
1937	H.N.	30	7	1937	F.G.	31	6
1937	A.L.	24	1	1937	W.F.	33	2
1937	H.E.	27	4	1938	E.S.	34	3
1937	A.W.	28	2	1938	R.L.	33	6
1938	F.S.	29	2	1938	C.C.	35	1
1938	H.S.	33	3	1938	A.B.	36	2
1938	G.L.	33	2				

* Consecutive pregnancies.
† Consecutive pregnancies.

Studies in Vaginal Fluid

BY

NORMAN LISSIMORE AND DAVID W. CURRIE.

PAPER I.

PATHOLOGICAL CONSIDERATIONS.

IN recent years the parasitology of the vagina has become a subject of increasing interest and exploration. Doubtless the chief cause of this lies in the re-discovery of the Trichomonas after almost a century of neglect and the apparent establishment of one of these organisms as a human pathogen following the work of Greenhill, Andrews, Kleegman and others. Apart from its relation to vaginitis, it is likely that in the near future some emphasis will be laid on the effects of this organism in the male, whether as a cause of active disease, or in the creation of mere carriers or agents of infection of women. For example, Drabkin[1] of St. Louis quotes two cases of presumptive re-infection of wives by their husbands, although we must place on record that in over 100 microscopical examinations of semen we have not yet encountered the trichomonas. Notwithstanding the negative finding, however, our youngest case, a girl aged 14, sent with a profuse discharge following criminal assault, was found to have a vaginal fluid teeming with trichomonas vaginalis without any Neisserian infection. Certainly a wide field of research has been made available by the seeming elevation of the trichomonas to the status of a human pathogen.

For some time past it has been evident to us that both the presence and absence of trichomonas vaginalis are related to other observable appearances, physical and chemical, in the vaginal fluid. Green-Armytage[2] has already referred to two types of leucorrhoea, the non-infected or normally acid type, and the infective, less acid, or even alkaline type. We have undertaken our investigation to relate, if possible, the changes observed in trichomonas or other parasitic infections. In addition to the variations from the normal high acidity our interest has been engaged on the presence or absence of glycogen, the presence or absence of the bacillus of Döderlein (both normal components of the vaginal fluid), and the concomitant bacteria which range from normal to undoubted factors of vaginal and cervical sepsis, since we believe all these factors to be interrelated.

The subject of our investigation has been in all cases that fluid which can be removed from the vaginal vault with a Volkmann spoon. The volume of this fluid varies. In health it is relatively scanty, but we have always been able to obtain 0.2 of a cubic centimetre, an amount adequate for examination. In disease it may be very copious indeed. Apart from these wide quantitative variations, there are also wide qualitative variations from the white, semi-solid, curded milk appearance in health, to the purulent, yellow fluid of infection. Numerous intermediate varieties exist; for example, the thin foamy yellowish fluid of trichomonas infection, and the mucoid fluid of cervicitis.

Concerning the origin of the vaginal fluid in health there is, it appears to us, still some confusion. Many authors refer to vaginal secretion, although it is commonly held that the vaginal epithelium is normally without glands. Some writers, for example W. Shaw,[3] say that the fluid is derived from two sources, (*a*) the cervical mucous glands, and (*b*) a transudate through the vaginal epithelium. The evidence for this transudation is chiefly of a histological character. Cruikshank,[4] using the Best carmine technique, has proved the presence of glycogen in the cells of the vaginal epithelium, particularly those of more superficial layers: this author has shown that intracellular glycogen occurs in female infants for some time after birth, being absent at 15 months, and returning at puberty, just prior to the onset of menstruation. Further, Muira, quoted by Cruikshank above, has correlated this intracellular glycogen with ovarian function, showing that it disappears at the menopause, whether natural or artificial. In regard to the correlation with ovarian function, Cruikshank explains the presence of glycogen in new-born infants by a carry-over in their blood of ovarian hormones derived from the mother, just as the same cause is held to explain neonatal leucorrhoea. These views, and the evidence in support of them, recommend themselves highly to our acceptance, particularly as we have reason to associate an ovarian dysfunction with some cases of vaginal discharge. If they are true, vaginal glycogen would appear to be the product, at first or second hand, of ovarian hormone activity. To the present authors, however, it appears that two other explanations of vaginal glycogen should be considered. These are not necessarily antagonistic to the above views. Firstly, that it is, in part at least, a product of the natural disintegration of the normally shed vaginal epithelial cells. Secondly, that it is one of the products of the endometrial glandular cells during their secretory phase, passing to the vagina

to be partially absorbed by the covering cells. Such a conception is perfectly compatible with the increase of intracellular glycogen observed in the secretory phase. The absence of glycogen from early infancy and during the pre-menstrual years, and its relative absence during post-menstrual life, would be equally well explained. Further, we incline to the belief that the chief function of glycogen in the vagina is as the pabulum of the physiological vaginal flora, and with these (as a result of fermentation) the source of the normal vaginal acidity. This is, in part at least, but a reversion of Döderlein's original view of the function of the bacillus he described, although he postulated a cervical glandular origin for the glycogen. It is only during recent years as a result of the demonstration of glycogen within the vaginal epithelium that the theory of cellular transudation has been advanced, and we shall use the non-committal terminology of "vaginal fluid" to describe the subject of our investigation.

We have collected 105 cases for the present report and, as normal data, have adopted the following standards:

Physical characters:

(*a*) A volume of less than $\frac{1}{2}$ c.c.
(*b*) A semi-fluid consistence.
(*c*) A whitish or greyish colour.
(*d*) Little or no smell.

Chemical characters:

(*a*) Glycogen should be demonstrable.
(*b*) The *p*H should be between 4 and 5.

Microscopical characters:

(*a*) Döderlein's bacilli should be numerous.
(*b*) Epithelial cells should be numerous.

In addition to the above, certain findings in a normal fluid will be negative or nearly so. For example, although a few degenerated leucocytes may be found, frank pus will be absent. Streptococci should be absent, or nearly so. One may find moderate numbers of Gram-positive cocci (enterococci, staphylococci) bacilli of the smaller diphtheroid type and a few yeasts, but in normal fluid epithelial cells and bacillus Döderlein should dominate the microscopical picture.

TECHNIQUE.

In all cases the fluid has been withdrawn with a warm, sterile Volkmann's spoon, and whenever possible the vagina has been exposed with a warm unlubricated speculum. Examination of the fluid has been proceeded with at once, whenever possible.

Microscopical Examination.

(*a*) A simple wet film of the fluid diluted if necessary with warm sterile normal saline is made. Such dilution is unnecessary as a general rule. When present, the trichomonas is easily discernible as a greenish, more or less rapidly motile organism. It is possible that too much has been made of the necessity to keep the slide warm. On numerous occasions flagellar motility and the undulatory membrane, which features are diagnostic, are easily demonstrated after hours at room temperature when evaporation and drying have been prevented. The implication is that an enforced delay to examine would not exclude the possibility of a diagnosis. The pleomorphism of the trichomonad must be borne in mind, and with other writers, for example, Goodall, Anderson and McPhail,[5] we must lay very great stress on this. Any notion of a uniform size or morphology must be abandoned. Not only have we seen giants the size of epithelial cells, but also organisms as small almost as a spermatozoon, the latter exhibiting a motility so energetic that cooling has been necessary to identify them. Here the possibility of infection with multiple strains of trichomonas must be borne in mind since we have encountered large and small in the same specimens.

(*b*) Films are dried and fixed by mild heat and stained by the following modified Gram technique:

1. Stain with watery methyl violet 6B for 1 minute; wash with plain water.
2. Mordant with Gram's iodine, 1 minute.
3. Decolorize with industrial methylated spirit to the optimal end point learned only by experience.
4. Counterstain with dilute fuchsin (Z–N, 1 in 20 with aqua distillata) for 1 minute.

Chemical Examination.

(*a*) *Hydrogen-ion concentration.* A range of British Drug House capillometers is used. In the first place the approximate *p*H is estimated with the four-eleven indicator first suggested to us by Green-Armytage. We made our final determination with a capillometer of a narrower and more accurate range, for example, brom-cresol purple, 3.6 to 5.2,, brom-thymol blue 6.0 to 7.6. It will happen sometimes that the opacity of the fluid will obscure the reading, but if the fluid is centrifuged in a capillary tube an accurate reading is easily made with supernatant fluid.

(*b*) *Glycogen.* We used two methods, of which the former is much more sensitive to detect free glycogen, the latter more sensitive to detect cellular glycogen:

(1) Equal volumes of vaginal fluid and 1 per cent of Lugol's iodine are mixed in a capillary tube, and the colour compared with ½ per cent of Lugol's iodine in a capillary tube of similar thickness. Darkening of colour towards a deep sepia indicates proportionate glycogen. A normal fluid so treated will develop a deep sepia colour If the opacity of the fluid obscures the reading, we have found centrifugalization to be unreliable, since on occasion the iodine will be mostly bound in the epithelial cells and the supernatant fluid will have the same or a lighter colour than the control tube.

(2) A wet film is made of equal parts of Lugol's iodine and vaginal fluid, covered with a No. 1 slip and examined with one-sixth inch objective. By this means it will be frequently found that the glycogen resides chiefly in the epithelial cells. We have rarely found the first test positive when the second has been negative, but we regard both of the tests as necessary to exclude glycogen in doubtful cases.

Culture Methods.

Aerobic cultures have been made on blood-agar film plates, that is, a film of 5 per cent blood-agar poured on to a previously cooled agar plate. On such a thin film of blood readings are much sharper than on a thicker and more opaque blood-agar plate. Some anaerobic cultures have been made to exclude or identify a doubtful bacillus Döderlein. When a bacillus Döderlein is marked as positive in the microscopical examination and not mentioned in the culture, its presence has been assumed from the characteristic morphology in the film only.

Findings and Discussion.

1. Normal Findings.

In 6 cases, 5.7 per cent, a qualitative abnormality was not found. The findings are listed below:

Table I

Case	Microscopy				Chemistry		Culture
	Tr. Vaginalis	Pus	Epithelial cells	B. Döderlein	*p*H.	Glycogen	
1 Miss C.	–	–	++	+	4.2	++	Staph. albus
2 Mrs. W.	–	–	++	+	4.0	++	Staph. albus b. coli (a few colonies)
3 Mrs. D.	–	–	++	+	4.6	++	Staph. albus diphtheroid bacilli
4 Mrs. C.	–	–	++	+	4.2	++	Staph. albus
5 Miss W.	–	–	++	+	4.8	++	Staph. albus only
6 Mrs. F. W.	–	–	++	+	4.0	+++	Staph. albus

Commentary on Table I.

These 6 patients complained of discharge. Two explanations suggest themselves: firstly, that we were dealing with a quantitative excess of a qualitatively normal fluid caused by an increase of ovarian hormones (cf. the explanation of neonatal leucorrhoea), and, secondly, increased scrupulosity in the patients regarding their cleanliness. Three of the patients were not of the hospital class.

2. Trichomonas Positive Cases.

Such cases numbered 71, 66.9 per cent, and supplementary findings are given below:

Table II

Microscopy						Chemistry			Culture					
Pus		Epithelial cells and debris		B. Döderlein		*p*H	Glycogen							
Abundant	Scant or absent	Abundant	Scant or absent	Present	Absent	Average	Present	Absent	Haemolytic streptococcus	Staphylococcus aureus	Streptococcus viridans and non-haemolytic	Enterococcus	B. coli	Neisser
28	43	19	52	1	70	5.99	13	58	6	21	5	1	5	0

Commentary on Table II.

(*a*) *Microscopy.*

1. Pus was abundant in 39.4 per cent of cases, scant or absent in 60.6 per cent. Of this latter series of 43 cases pus was absent entirely in 13 so far as wet and dry films could determine, yet of these 13 cases trichomonas were abundant in 12. It follows that the flagellate is not pyogenic in its unaided effects, and that when pus is present with it it is to be explained by secondary (or, at any rate, additional) infection.

2. *Epithelial cells and debris.* In about 73 per cent of trichomonas infection this normal epithelial component of the vaginal fluid is much diminished, that is, normal vaginal desquamation is impeded.

3. *Bacillus of Döderlein.* In the single case in which this organism was found the trichomonas was the only observed abnormality. Pus was absent, epithelial content normal, *p*H 4.4, and

glycogen abundant. Nevertheless, in 98.5 per cent of our trichomonas positive series the bacillus of Döderlein was absent.

(*b*) *Chemistry.*

1. *Hydrogen-ion concentration.* It is accepted that trichomonas is associated with a low acidity, indeed Bender (quoted by Goodall, Anderson and McPhail) gives the optimum *p*H range for the organism as 7.0 to 7.6. It will be observed that the latter figure is more alkaline than human blood. In our series the average figure of 5.99 is the mean of a variation from 4.4 to 7.0. The lower figure is the Döderlein positive case described above, and it is notable that the next lowest figure was 5.2, which represents a substantial rise.

2. *Glycogen.* This normal constituent was absent about four and a half times as frequently as it was present.

3. TRICHOMONAS NEGATIVE CASES.

Thirty-four cases.

TABLE III

MICROSCOPY				CHEMISTRY		CULTURE								
Pus.		Epithelial cells and debris		B. Döderlein		*p*H	Glycogen							
Abundant	Scant or absent	Abundant	Scant or absent	Present	Absent	Average	Present	Absent	Haemolytic streptococcus	Staphylococcus aureus	Streptococcus viridans and non-haemolytic	Enterococcus	B. coli	Neisser
15	19	20	14	13	21	5.5	20	14	4	19	4	2	8	1

Commentary on Table III.

(*a*) *Microscopy.*

1. Pus was abundant in 44.1 per cent. The 19 patients in whom it was scant or absent include the 6 in whom no qualitative abnormality was found; of the remaining 13 cases pus was present in small amounts in 11 and pyogenic bacteria were also found.

2. *Epithelial cells and debris.* There was much less diminution of these constituents than in the trichomonas positive series.

TABLE IV

TRICHOMONAS NEGATIVE.

DODERLEIN POSITIVE.						DÖDERLEIN NEGATIVE.					
Case	Pus	Epithelium	*p*H	Glycogen	Culture	Case	Pus	Epithelium	*p*H	Glycogen	Culture
1	–	++	4.2	+		1	++	++	5.8	+	(age 53). Staphylococcus aureus
2	–	++	4.0	+		2	++	++	5.5	–	B. coli, staphylococcus aureus, non-haemolytic streptococci
3	–	++	4.6	+		3	+	+	5.5	+	Staphylococcus aureus
4	–	++	4.2	+		4	++	–	8.0	–	Staphylococcus aureus abundant
5	–	++	4.8	+	Nothing significant	5	++	–	6.5	–	Neisseria abundant, staphylococcus aureus abundant
6	–	++	4.0	+		6	++	–	6.25	–	B. coli, staphylococcus albus, enterococcus
7	–	++	4.5	+		7	++	+	6.25	–	Staphylococcus aureus abundant, staphylococcus albus abundant
8	–	++	4.5	+		8	++	–	6.8	–	Haemolytic streptococcus, b. coli
9	–	++	4.1	+	Staphylococcus aureus (a few colonies)	9	++	–	6.5	–	Staphylococcus aureus
10	+	++	4.6	+	Staphylococcus aureus	10	++	+	6.25	–	Staphylococcus aureus
11	–	++	4.8	+	Nothing significant	11	+	++	6.0	+	Staphylococcus aureus
12	–	++	4.2	+		12	++	++	6.25	–	Haemolytic streptococcus, staphylococcus aureus
13	++	–	6.25	–	Haemolytic streptococcus, Staphylococcus aureus	13	–	++	5.5	+	B. coli (spinster, aged 60)
						14	+	(+)	6.9	–	Staphylococcus aureus (post-hysterectomy)
						15	+	++	5.5	+	Staphylococcus aureus
						16	–	+–	5.5	–	Enterococcus, b. coli
						17	+	+	5.8	+	Staphylococcus aureus, b. coli (age 53 years)
						18	++	++	5.0	+	Nothing significant
						19	++	++	6.5	–	Staphylococcus aureus
						20	++	+	6.75	–	Staphylococcus aureus, non-haemolytic streptococcus
						21	++	–	7.0	–	B. coli, staphylococcus aureus, haemolytic streptococcus

TABLE V

TABLE V

TRICHOMONAS NEGATIVE.

Glycogen.

GLYCOGEN PRESENT.						GLYCOGEN ABSENT.					
Case	*p*H	Pus	Epith-elium	B. Död.	Significant cultural finding.	Case	*p*H	Pus	Epith-elium	B. Död.	Significant cultural finding.
1	4.2	–	++	+	Nil	1	6.25	++	–	–	Haemolytic streptococcus, staphylococcus aureus
2	4.0	–	++	+	Nil	2	5.5	++	++	–	B. coli, staphylococcus aureus, nonhaemolytic streptococcus
3	4.6	–	++	+	Nil	3	8.0	++	–	–	Staphylococcus aureus abundant, streptococcus viridans
4	4.2	–	++	+	Nil	4	6.5	++	–	–	Neisseria abundant, staphylococcus aureus abundant
5	4.8	–	++	+	Nil	5	6.25	++	–	–	B. coli, staphylococcus aureus enterococci
6	4.0	–	++	+	Nil	6	6.25	++	+	–	Staphylococcus aureus abundant, staphylococcus albus abundant
7	4.5	–	++	+	Nil	7	6.8	++	–	–	Haemolytic streptococcus, b. coli
8	4.5	–	++	+	Nil	8	6.5	++	–	–	Staphylococcus aureus
9	4.1	–	++	+	Staphylococcus aureus, a few colonies	9	6.25	++	+	–	Staphylococcus aureus
10	4.6	+	++	+	Staphylococcus aureus	10	6.25	++	++	–	Haemolytic streptococcus, staphylococcus aureus
11	4.8	–	++	+	Nil	11	5.5	–	+	–	B. coli, enterococcus
12	4.2	–	++	+	Nil	12	6.5	++	++	–	Staphylococcus aureus
13	5.8	++	++	–	Staphylococcus aureus (aged 53)	13	6.75	++	+	–	Staphylococcus aureus, nonhaemolytic streptococcus
14	5.5	+	+	–	Staphylococcus aureus	14	7.0	++	+	–	B. coli, staphylococcus aureus, haemolytic streptococcus
15	6.0	+	++	–	Staphylococcus aureus						
16	5.5	–	++	–	B. coli (spinster, aged 60)						
17	6.9	+	(+)	–	Staphylococcus aureus (post-hysterectomy)						
18	5.5	+	++	–	Staphylococcus aureus						
19	5.8	+	+	–	Staphylococcus aureus						
20	5.0	++	+	–	Nil						

3. *Bacillus of Döderlein.* The figures are in sharp contrast with those of the trichomonas positive cases. In the following table the presence or absence of the bacillus is related to the other findings. Only significant bacteria are listed in the culture findings.

Table IV demonstrates that in a vagina free from trichomonas vaginalis the presence of the Döderlein bacillus is associated with an average *p*H of 4.52, co-existing glycogen and the epithelial cells which harbour or produce it, a relative absence of pyogenic bacteria and pus. The absence of this bacillus is, *per contra,* associated with a *p*H of 6.15, diminished glycogen epithelial cells, abundant pyogenic bacteria and consequently pus.

(*b*) *Chemistry.*

1. *Hydrogen-ion concentration.* The average figure is lower than in the trichomonas positive series, 5.5 against 5.99. The range is greater, however, 4.0 to 8.0, although little significance may attach to this since the lower end includes normal fluid. The higher end is of some significance in that our highest *p*H observed is in a trichomonas negative case, a case of repeated old Neisserian infection, in which, although Neisseria were not demonstrated, pyogenic organisms were numerous, pus abundant, and the Döderlein bacillus and glycogen absent

2. *Glycogen.* The absence of this normal constituent is much less encountered than in the trichomonas positive series. Table V (p. 681) relates its presence and absence to other features.

Commentary.

The presence of glycogen is associated with:
(*a*) A normal *p*H reading; 4.9 is the average of our range.
(*b*) The bacillus of Döderlein ; in 60 per cent of our series.
(*c*) An absence of pus in the majority of cases.
(*d*) A relative absence of pyogenic bacteria.
(*e*) A good vaginal content of epithelial cells.

Per contra, the absence of glycogen is associated with:
(*a*) A high *p*H reading; 6.45 is the average of our range.
(*b*) Absence of bacillus Döderlein.
(*c*) Presence of pus.
(*d*) Presence of pyogenic bacteria.
(*e*) A poor vaginal content of epithelial cells.

SUMMARY.

1. A series of 105 cases of vaginal discharge is examined. The technique of the examination of the patient, the removal and examination of the fluid are described.

2. A small proportion of the cases, 5.7 per cent, show no qualitative vaginal fluid abnormality. Two explanations of this are offered.

3. The majority of the cases, 66.9 per cent, are the hosts of trichomonas vaginalis.

4. The trichomonas vaginalis is not pyogenic but is associated with a lowering of the normally high acidity of the vaginal contents, and the removal of one of the most powerful barriers to infection by pyogenic invaders, of which the Staphylococcus Pyogenes Aureus is by far the commonest in our series. This accounts for the frequent association of the flagellate with pus, secondary infection being more usually present. In our view there are two possible explanations of this association of the flagellate with decreased activity:

(*a*) The trichomonas is antagonistic to the bacillus Döderlein. It also impedes the normal desquamation of vaginal epithelium. Thus both factors associated with normal vaginal acidity, namely, bacillus Döderlein and glycogen, are reduced or absent.

(*b*) The acidity of the vagina suffers great antecedent reduction by at least two natural factors, namely (1), the advent and menstrual lochia during periods, and (2), the deposition of semen during intercourse. The trichomonas, finding once again a medium of a *p*H agreeable to its existence, readily re-establishes itself. It is thus not necessary to postulate direct infection from the male during intercourse. Either of these two factors would explain the reappearance of trichomonas after apparent cure.

5. In the 33.1 per cent of cases in which trichomonas is absent pyogenic infection explains the qualitative abnormalities of the vaginal fluid, and, as in the trichomonas positive cases, the Staphylococcus Pyogenes Aureus appears to be the commonest invader.

6. Absence of symbiosis of the bacillus Döderlein with pyogenic bacteria is also observed, but in a lessened degree than in the trichomonas positive cases. Similarly, vaginal epithelial desquamation is less impeded than by trichomonas vaginalis, the glycogen content less diminished. As a result there is not so great a lowering of the vaginal acidity from normal.

7. The inter-relations between both the normal and abnormal constituents of the vagina are emphasized.

8. We have observed glycogen, but not Döderlein's bacillus, in a married woman of 53 years, a spinster of 60 years, a woman who had previously undergone vaginal hysterectomy. Unless explained by residual ovarian hormones these findings run counter to those of Muira and Cruikshank (noted earlier), but until repeated on a much larger number of post-menopausal subjects should be considered with reserve. They do not counter the view that glycogen is a product of normal vaginal epithelial desquamation.

In conclusion, we desire to thank the Honorary Staff of the Hospital for Women at Leeds for their co-operation, and in particular Mr. John Asbey for assistance with the laboratory investigations.

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The Pathology of Hyperemesis and Vomiting of Late Pregnancy

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IN the course of routine work it became evident that the textbook descriptions of the pathological lesions of hyperemesis or late vomiting were somewhat misleading. It is often said that the standard findings are centrilobular necrosis of the liver and degeneration or necrosis of the epithelium of the renal tubules. These views stand in need of reconsideration. Saenger[1] made a review of the pathology of hyperemesis, but most of the recent surveys are naturally devoted more to the clinical than to the pathological aspects: Frey,[2] Anselmino,[3] Kehrer,[4] Schjøtt-Rivers.[5] A study was, therefore, made of cases which had come to post-mortem in this hospital within the last 10 years, and in which adequate histological material had been preserved. The patients who had died later than 24 hours post-partum are deferred for subsequent discussion; such cases are unsuitable for primary study as the pathological changes relating to the vomiting may have passed off or become obscured by the lesions of complicating diseases. The remaining 32 patients died as a direct result of hyperemesis or of vomiting of late pregnancy, either before or within 24 hours after delivery. They are free from interfering factors, and are sufficiently numerous to form a basis for conclusions.

HYPEREMESIS GRAVIDARUM.

Clinically, all the 19 patients included under this heading showed the typical syndrome: severe vomiting beginning from the fourth to the eighth week of gestation and continuing afterwards, tachycardia, low blood-pressure, ketonuria, and some loss of body fat and fluids; some of the dehydrated patients also had a high nitrogen retention in the blood, involving urea, uric acid, and creatinin. When vomiting had lasted for over 6 weeks there was sometimes slight jaundice. Most of the patients had undergone surgical induction or hysterectomy under gas-oxygen

or ether; chloroform had not been used in any case. Death occurred between the ninth and twenty-second weeks; the final stages followed either of two courses:

(*a*) In 6 cases the vomiting continued under medical treatment, and the pulse-rate steadily increased. Surgical intervention was therefore resorted to, and this was followed either by severe shock or by coma, with death in a few hours.

(*b*) In 13 cases, after the hyperemesis had lasted for 4 to 12 weeks, the vomiting was controlled or arrested by treatment, but the pulse-rate remained high and there usually were nystagmus and tenderness of leg muscles. A cerebral syndrome then developed, apathy, dullness, drowsiness, or sometimes great loquacity; more severe ocular symptoms, such as squint, diplopia, retinal haemorrhages, partial or complete blindness; less frequently paralysis of the soft palate or huskiness of the voice; and mental confusion passing into coma, which sometimes lasted for a day or two before death. The period from the onset of cerebral symptoms until death varied; it was sometimes 7 days or more, but occasionally only about two days. Surgical intervention appears to have hastened death in some of the cases.

At autopsy there was usually some indication of recent loss of weight but rarely any extreme emaciation; most of the patients had 2 or 3 centimetres thickness of fat in the anterior abdominal wall. There was not any constant relation between the amount of weight lost and the duration of the pregnancy or of the vomiting; among patients dying between the ninth and fourteenth weeks, 3 were recorded as emaciated and 3 as well nourished; among those dying at from the fourteenth to the twenty-second weeks, 3 were recorded as emaciated and 4 as well nourished. This does not imply that there is not a loss of weight in the individual cases.

Neither oedema nor unusual lack of fluid was found in any of the cases; it should, however, be noted that nearly all the patients had had much treatment with glucose-saline, either intravenously or rectally, before they died. Six of the patients had slight jaundice and one moderate jaundice; the jaundice in the last case was due to the obstruction of the common bile duct by tuberculous glands.

The heart was notably small, ranging from 170 to 270 gm., with a mean weight of only 220 gm. It was usually much smaller than would have been expected from the amount of fat in the body; the atrophy was almost as marked in the 7 well-nourished patients (mean heart-weight, 230 gm.) as in the 6 emaciated patients (mean heart-weight, 215 gm.) There was a more definite

correlation between the atrophy and the duration of the vomiting; the mean heart-weight was 260 gm. in patients who had had severe vomiting for up to 1 month, 220 gm. for 1 to 2 months, and 200 gm. for over 2 months.

In 4 cases there were small subendocardial haemorrhages on the left interventricular septum; 3 of these patients died of post-operative collapse (Sheehan[6]). Microscopically the heart did not show any obvious lesions apart from these haemorrhages.

The lungs showed various non-specific conditions such as early broncho-pneumonia or oedema. In a few cases following operative interference there were multiple small haemorrhages in the pulmonary tissue. In 3 cases there was a remarkable ballooning of the lungs with air so that they bulged from the opened pleural cavities, but an explanation could not be found for this, apart from a presumed bronchiolar spasm.

The liver was usually rather small. This was more marked in patients without jaundice (mean weight, 1210 gm., range 910 to 1660 gm.) than in patients with jaundice (mean weight 1420 gm., range 1170 to 1670 gm.) These figures may be compared with those of 20 control patients dying of shock at delivery (mean weight 1600 gm., range 1230 to 2200 gm.) There was also a marked yellowness of the liver in some cases; a correlation of naked-eye and histological findings indicates that this colour was due to pigment rather than to fat.

Microscopically there sometimes was a fatty change in the liver. The affected cells had a quite constant appearance: one large or a few medium-sized vacuoles full of fat occupied most of the cytoplasm, and the nucleus remained healthy (Figs. 1 and 2). This change was centrilobular and involved a quarter to a half of the lobule in 8 cases (5 moderate to slight, and 3 only traces); it was localized to the portal region in 2 cases, and was distributed throughout the whole lobule in 2 cases. In the remaining 7 cases, fat was entirely absent. It was not possible to trace any relation between the occurrence of fat and any other pathological findings or clinical or therapeutic details. In many of the cases there was some excess of pigment at the centre of the lobules, either in the hepatic cells or Kupfer cells. In some of the smaller livers, the lobules and the individual cell-columns appeared rather smaller than usual.

The kidneys had a weight range of 110 to 230 gm. each, with a mean weight of 140 gm. (20 normal pregnant patients dying of shock had kidneys weighing 110 to 180 gm. each, with a mean weight of 150 gm.) The kidneys sometimes showed pallor of the

cortex and in one patient there was slight early pyelonephritis. Otherwise there were not any gross naked-eye changes, and the ureters were not dilated.

Microscopically, out of 15 kidneys of which sudan-stained sections are available, 5 had a well-marked and 3 a moderate fatty change localized to the mitochondrial zone of the first convoluted tubules and present in every first convoluted tubule along its whole length, but not in the descending spirals (Fig. 3). This change was not seen in any patients who had received ample treatment with intravenous glucose for a few days before death. It was, however, present in most of those who had only glucose-saline *per rectum*, and was thus more common in patients who died more than four years ago. It was not found possible to relate the fatty change to any other clinical or pathological findings apart from the factor of glucose administration.

In the 9 cases in which the tissues were fixed within 2 hours after death, the glomeruli and the tubular epithelium were normal (Fig. 4) apart from the fatty change described, except that in 2 cases the first convoluted tubules had rather wide lumina and an associated shallowness of the epithelium. Cases in which the post-mortem examination was delayed showed the usual changes due to post-mortem autolysis and corresponding in degree to the time that had elapsed after death.

The suprarenal did not show any lesions. The cortical lipoid was always in large amount, and filled the entire cortex except in 3 cases. These three patients died rather early in the pregnancy (9 to 12 weeks) and had lipoid only in the outer half to three-quarters of the cortex.

The alimentary tract rarely showed any gross abnormalities. Small petechial haemorrhages were occasionally present in the gastric mucosa, but detailed histological examination of the stomach has not been made. One patient had a terminal ulcerative colitis.

The spleen and pancreas were normal. In one case, previously mentioned, there was a mass of tuberculous lymph glands in front of the pancreas pressing on the common bile-duct and causing jaundice.

The uterus and ovaries were normal apart from a retroversion in one case and an adhesion of one ovary to the pelvic wall in another case.

The brain was examined in 11 of the patients. There was not any gross oedema; the weight ranged from 1100 to 1310 gm., with a mean weight of 1230 gm.; these figures may be accepted as normal.

Specific changes in the brain were not found, or not recognized, until recently. The work of Campbell and Biggart[7] has, however, indicated the need for careful search in these cases for the lesions of Wernicke's encephalopathy. Only 2 cases in the present series have been examined with this in mind. The first showed the typical lesions of capillary walls and tiny haemorrhages of symmetrical distribution in the corpora mammillaria, in the walls of the third ventricle formed by the thalami, in the inferior corpora quadrigemina and in the floor of the fourth ventricle (Fig. 5); the patient died with blindness, retinal haemorrhages, palatal paralysis and coma. The second patient had the haemorrhages in the corpora mammillaria only (Fig 6), and the capillary lesions were not found; she had squint, partial blindness and terminal coma. In both cases there was degeneration of nerve cells in the inner half of the olivary nuclei.

Retinal haemorrhages were present in 3 of the cases, but they were not studied histologically.

Vomiting of Late Pregnancy.

For comparison with hyperemesis, a similar study was made of deaths associated with vomiting of late pregnancy. The vomiting had been severe for at least one week and usually for several weeks before delivery or death. In most cases it was of sudden onset late in the second half of pregnancy; a few of the patients had had mild vomiting throughout the pregnancy, but not in any way severe until the later stages.

One very distinctive group is separated from the others for consideration in a later paper: this consists of patients with a clinical syndrome which is usually interpreted as acute yellow atrophy. After eliminating this group, there remain 13 patients with late vomiting who died either before or within 24 hours after delivery. Certain aetiological factors were found in many of these, either before or after death. Five had pyelitis or ulcerative colitis, 4 had pre-eclampsia, one had marked anaemia; in the other 3 cases the vomiting appeared to be idiopathic. The various pathological lesions related to these specific diseases will be omitted from the following discussion, as they are not essential to the pathology of vomiting.

At autopsy the patients showed all gradations from extreme obesity to emaciation. Jaundice was never present, but oedema was not uncommon.

The heart never showed the atrophy which is seen in hyperemesis. It had a weight-range of 240 to 360 gm. with a mean

weight of 290 gm.; this is of full normal size. The weight of the heart did not show any relation to the duration of the vomiting or to the degree of emaciation. In two cases the left ventricle was grossly dilated.

The liver was also of normal weight, both in range and mean. In five cases there was some fat in the liver forming large vacuoles; the affected cells had normal nuclei, and the appearances resembled those described in certain of the livers in hyperemesis. The fat was centrilobular in two cases, periportal in one, and in the other two evenly distributed throughout the lobule. True degenerative changes could not be found in any of the livers.

The kidneys frequently showed the specific lesions of hypertensive toxaemia or pyelitis, but these changes will not be considered here. Of the 9 cases in which sudan-stained sections of the kidney were available, 6 showed the same fatty change in the mitochondrial zone of all the first convoluted tubules as was noted in hyperemesis. This was very heavy in 2, moderate to slight in the other 4 cases. In these patients the vomiting had been severe for 1 to 5 weeks; intravenous glucose had not been given to any of them except during the last 24 hours.

Eight of the kidneys had been fixed within two hours after death. Excluding the changes just noted, the glomeruli and tubules were normal in 7; in the eighth case there was some swelling due to non-fatty vacuolation in the epithelium of the first convoluted and spiral tubules. In the other 5 cases the post-mortem examination was delayed and the kidneys showed the usual autolytic changes.

The suprarenal had full lipoid throughout the whole depth of the cortex except in one case, an ulcerative colitis with prolonged pyrexia.

The lungs, the abdominal viscera and the pelvic viscera did not show any specific changes.

The brain was of ordinary weight and did not appear abnormal to the naked eye; in the last case, in which the patient died with the same terminal cerebral syndrome as has been described in connexion with hyperemesis, a microscopic examination of the corpora mammillaria and of the thalami showed quite typical haemorrhagic lesions of Wernicke's encephalopathy.

Discussion and Literature.

The significance of the fat in the first convoluted tubules of the kidney may be considered first. As a control, sudan-stained sections of the kidneys have been studied from about 200 post-

mortem examinations on obstetric patients who had not had hyperemesis or late vomiting. In a few cases there was fat in certain isolated first convoluted tubules; this is an entirely different process which will not be considered here. In only 4 cases was there any general fatty change in the first convoluted tubules of the type seen in the cases of vomiting. Three of these were deaths from obstetric shock within 4 hours after prolonged labour (2 to $3\frac{1}{2}$ days); the other was a status epilepticus treated for several hours with chloroform on the day before death. Intravenous glucose had not been given to any of these 4 patients until shortly before death. It will be noted that all the patients in whom the fatty change has been found have strong presumptive evidence of acidosis, that it is not found if adequate glucose has been given for 2 or 3 days before death, and that it can probably develop in about this time. Though the evidence is inconclusive, the most reasonable interpretation is that the fatty change seen in some of the cases with vomiting is only a result of acidosis. The presence of fat in the mitochondrial zone is, however, probably associated with some disturbance of function of the first convoluted tubules, and thus may possibly play a part in the nitrogen retention in certain of these cases. Other factors, such as anhydraemia and oliguria, are, of course, of importance in this regard.

The fatty infiltration of the liver is probably of less significance. It is quite unrelated to the presence of fat in the kidneys or to the amount of subcutaneous fat, to jaundice or to mode of death, or to treatment with glucose. In a series of control cases a similar accumulation of fat was quite frequently found, either centrilobular, periportal, or throughout the lobule; it was usually associated with puerperal sepsis of several days' duration. These cases of sepsis may involve a direct action of bacterial toxins on the hepatic cells, but the connecting link between them and the cases of vomiting is more probably a loss of weight due to inadequate food intake. On this view, the fat in the liver is merely an index of the mobilization of the reserves of body fat. Why it should occupy different parts of the lobule in different cases is not clear.

It will be noted that mention has not been made of centrolobular necrosis of the liver. This lesion was not found in a single case in the present series. Furthermore, the histological study did not provide any evidence to suggest that any fatty change in the liver progresses to a true cellular degeneration. These conclusions are supported by a study of the literature dealing with the hepatic and renal lesions. As with the cases studied personally,

the following references deal only with the changes found in patients with hyperemesis or late vomiting who died either before delivery or within 24 hours afterwards, and in whom the post-mortem examination included histological study. The earlier literature is discussed by Dirmoser[8] and will not be considered here.

Lindemann[9]
Liver. Fatty infiltration and cloudy swelling.
Kidney. Slight fat in broad ascending limbs. Degeneration of epithelium of convoluted tubules.

Lang[10]
Liver. Fatty degeneration.

Ewing[11] (Case 3)
Liver. Central fatty change.

Winter[12]
Liver. Much central fat.
Kidney. Basal fat in convoluted tubules.

Maxwell[13]
Liver. Much central fat.
Kidney. Considerable fatty change and parenchymatous degeneration.

Siemerling[14]
Liver. Central fat. Pigment in Kupfer cells.
Kidney. Fat in occasional straight tubules.

Henriksson[15]
Liver. Some central fat.
Kidney. Areas with basal fat in convoluted tubules. Areas with desquamation and necrosis.

Kobrinsky[16]
Liver. Some fat. Cloudy swelling.
Kidney. Cloudy swelling of tubules.

Rupp[17]
Liver. Very slight fat. Cells all separated.
Kidney. Necrosis of all cortical tubules except in subcapsular layer.

Benthin[18] (Case 2)
Liver. Fatty.
Kidney. Patchy desquamation and necrosis of tubular epithelium.

Frankl[19] (Case 1)
Liver. Central fat.
Kidney. Fat in convoluted tubules and loops. Some casts.

Bell[20] (Case 18)
Liver. Fatty.
Kidney. Slight pyelitis.

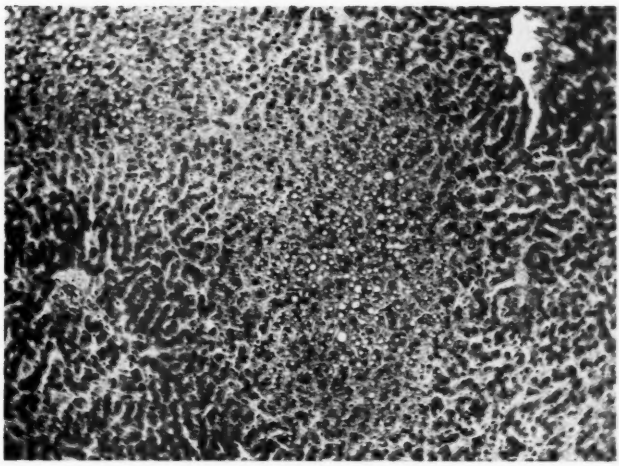

FIG. 1.
Liver in hyperemesis.
Fatty change at centre of lobules.

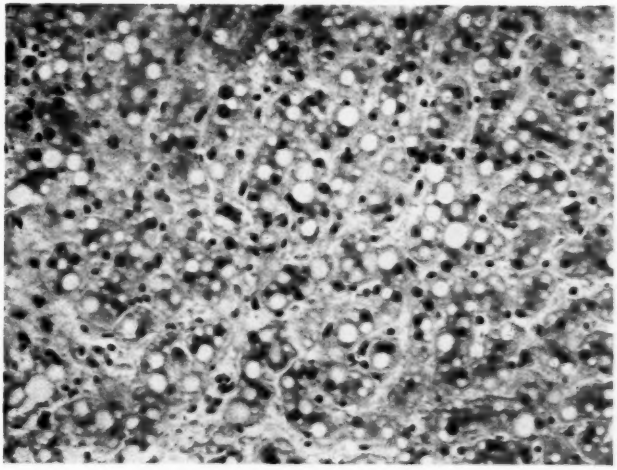

FIG. 2.
Liver in hyperemesis.
High power view of fatty change.

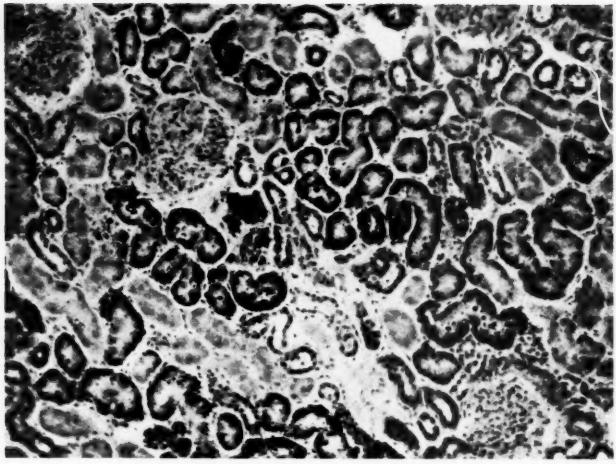

FIG. 3.
Kidney in hyperemesis.
Sudan stain. Fat in mitochondrial zone of first convoluted tubules.

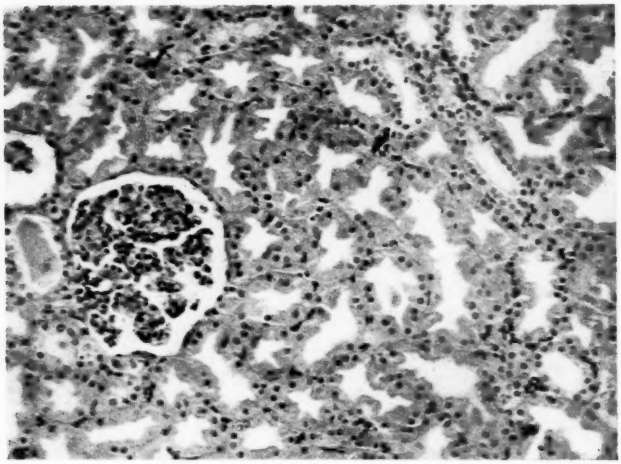

FIG. 4.
Kidney in hyperemesis.
Paraffin section. No abnormality.

FIG. 5.
Brain in hyperemesis.
Petechial haemorrhages in floor of fourth ventricle.

FIG. 6.
Brain in hyperemesis.
Petechial haemorrhages in corpora mammillaria.

Bell[20] (Case 20)
Liver. Cloudy swelling.
Kidney. Nil.

Harrison[21]
Liver. Areas of fat and cloudy swelling.
Kidney. Cloudy swelling and degeneration of tubules.

Berkwitz and Lufkin[22] (Case 1)
Liver. Minimal central fat.
Kidney. Moderate granular change in tubules.

Berkwitz and Lufkin[22] (Case 3)
Liver. Normal.
Kidney. Normal.

Kolbow[23] (three cases)
Liver. Central fatty infiltration.
Kidney. Fine fat in straight tubules.

Luikart[24]
Liver. Cloudy swelling.
Kidney. Cloudy swelling.

Pigeaud and Michelon[25]
Liver. Excessive pigment, otherwise normal.

Tillman[26] (Case 2)
Liver. Central fat and also some central cellular degeneration
Kidney. Cortical necrosis of rather peculiar type, with no thrombosis of vessels. Some fat in some convoluted tubules.

In the case of cortical necrosis of the kidney recorded by Tillman, the pathological description is quite reliable; the liver changes are similar to those seen in certain other cases of this type and cannot be regarded as due primarily to the hyperemesis. This case must, however, be set aside as exceptional. In a critical consideration of the other cases, many of the findings recorded as pathological lesions must be dismissed as merely the ordinary results of post-mortem autolysis. This applies particularly to descriptions of degeneration, desquamation, and necrosis of the renal tubular epithelium, or of separation of hepatic cells. Such changes can develop within a very few hours after death, and the necessity of early post-mortem examination cannot be over-emphasized. Details about the distribution of fat in the kidneys or liver are, however, less open to objection, as these changes are relatively unaffected by autolysis. The descriptions of fat in straight tubules in the kidneys probably refer to the broad ascending limbs. Fat in this site is seen in many patients who

die at or about delivery from any cause, and cannot be considered a specific lesion of hyperemesis. The histological changes in these organs which are recorded in the literature and which can be accepted as specific pathological lesions may thus be summarized as follows. The liver often contains some fat, either centrilobularly or with some other distribution, but does not show any degenerative changes or necrosis. The kidney sometimes has some fat in the first convoluted tubules, usually basal, but is otherwise normal. These conclusions agree with the findings of the present study.

Probably the most constant pathological finding in hyperemesis is the small size of the heart. A heart of 230 gm. is unusually large in hyperemesis and abnormally small in an ordinary pregnancy. The atrophy appears to progress according to the duration of the hyperemesis rather than to the degree of emaciation of the patient, and it seems possible that the hyperemesis exercises some trophic influence on the myocardium. This may be related to the marked tachycardia in these cases and the great tendency of these patients to collapse and die during operative interference. There is not any histological proof of the occurrence of a toxic myocarditis; Harrison records such a finding, but the histological appearances in his case are unconvincing. A corresponding atrophy of the heart is not seen in late vomiting, but the duration of the vomiting is usually less in these cases and there is often an additional complication such as hypertension.

The condition of the brain must still be considered *sub judice*. The lesions of Wernicke's encephalopathy can easily be overlooked in a routine autopsy in which specific search for them is not made. Particular attention has to be paid to certain small parts of the brain such as the corpora mammillaria, and microscopic examination is often required. It is only recently that the possible occurrence and significance of the lesions have been recognized, and the negative results of many earlier post-mortem examinations of the brain thus carry little weight. In the present series the lesions were found in the last three patients with the cerebral syndrome in which a deliberate search for them was made, but not in the earlier cases with ordinary examination of the brain. It remains for future study to show whether or not the lesions are always present in patients who have developed the cerebral syndrome. But, if they prove to be always associated, they will provide a very satisfactory explanation for the cerebral features and for many of the deaths. And, even if they are not constant, the possibility of a local vascular disturbance insuf-

ficient to produce recognizable histological changes must be borne in mind.

A thorough study of the Wernicke lesions has been made recently by Campbell and Biggart, who report 2 cases in vomiting of pregnancy (cases 8 and 9). Complete details about the pathology and literature will be found in that paper and will not be gone into here. Changes which were probably Wernicke lesions, though not recognized as such, have also been recorded previously in hyperemesis by Maxwell, Siemerling, Berkwitz and Lufkin (case 3), and Tillman (case 2). The lesions are also the standard pathological finding in the Korsakoff syndrome and also in deaths in coma following certain gastro-intestinal diseases, particularly carcinoma of the stomach. Most of these gastro-intestinal cases have had prolonged vomiting and inadequate food intake, and it appears that the Wernicke lesions in hyperemesis are the result of these factors. The case in early pregnancy recorded by Naujoks and Uffenorde[27] appears to have been due to simple lack of food with practically no vomiting. The question of an origin due to acute deficiency of vitamins or other substances, possibly aggravated by the demands of the foetus, or to some unknown toxin, is still unsettled and will not be discussed here.

The related conditions of toxic neuronitis or Landry's paralysis associated with hyperemesis are amply reviewed by Berkwitz and Lufkin and Schjøtt-Rivers.

The retinal haemorrhages are presumably of similar aetiology to the cerebral lesions. This change has been noted previously in hyperemesis by Guggisberg,[28] Allbeck,[29] Bell, Stander,[30] Berkwitz and Lufkin, Tillman, Anselmino, Randall and Wagener,[31] and Waterman.[32]

Pathological Findings in the Puerperium.

The patients who died later than a day after delivery have been excluded from the previous consideration owing to the possible complications during the puerperium. For comparison, however, a short summary may be given of the findings in 6 patients with hyperemesis and 7 with vomiting of late pregnancy who died between the first and ninth days of the puerperium, either with jaundice, sepsis, or cerebral symptoms.

The heart showed the same conditions as have been described earlier. After hyperemesis it weighed 180 to 240 gm., mean 210 gm.; after late vomiting it weighed 240 to 340 gm., mean 280 gm.

The liver varied according to the anaesthetic which had been used. In 4 patients the delivery was spontaneous without anaes-

thetic; the liver showed moderate centrilobular fat in 1, trivial centrilobular fat in 2, and was normal in the fourth. Four patients were delivered under gas-oxygen-ether; the liver showed moderate centrilobular fat in 1, moderate periportal fat in 2, and was normal in the fourth. Four patients were delivered under chloroform; the liver showed gross centrilobular necrosis in 2, who died 3 and 4 days after delivery, much centrilobular fat in 1, and fat throughout the lobule in the fourth. One patient was delivered under ether, but the anaesthesia was possibly induced by chloroform; she died 1½ days after delivery, and the liver showed an early degeneration of the centre of the lobules.

The kidneys did not show any obvious changes apart from lesions of pyelonephritis or of hypertensive toxaemia. Sudan-stained sections were studied in 5 cases but did not reveal any fat; all these patients had, however, had efficient treatment with intravenous glucose for a few days before death. Sudan-stained sections were not examined in any patients who had died after having been given chloroform.

The brain was examined in 5 cases without any macroscopic changes being found. A microscopic search for Wernicke lesions was made in only one case, a woman who died in coma 2 days after delivery: the specific changes were found in this brain.

The other organs did not show any lesions which could be related to the vomiting. Slight uterine sepsis or bronchopneumonia was occasionally noted.

Summarizing these puerperal findings it will be seen that (*a*) certain of the changes were the same as those found before delivery and were merely a continuance of them into the purperium; (*b*) certain of the changes that were probably present before delivery had been removed by treatment; for example, the fat in first convoluted tubules; (*c*) additional lesions were present, of which the most striking was the centrilobular necrosis of the liver. This was quite clearly produced by chloroform, and the patients with this lesion died with the clinical picture of delayed chloroform poisoning. The previous vomiting may have rendered these patients unusually sensitive to the toxic action of chloroform, but cannot be considered to have caused the hepatic necrosis.

Literature on Lesions found in the Puerperium.

It appears advisable to give a short review of the literature on the changes found in the puerperium after hyperemesis or late vomiting, since it is not generally recognized that several of the

most quoted standard references on hyperemesis actually deal with changes developing only after delivery as a result of complicating factors. This summary is limited to patients dying from the second to the sixth day after delivery, which has been, in all cases, a surgical abortion. Only the cases in which histological examination was made are considered.

The liver showed gross centrolobular necrosis, with fat in the remainder of the lobule, in 8 cases in which the patient died 2 to 4 days after the surgical abortion: Stone,[33] Opie,[34] Williams,[35] Strauss[36] (case 2), Ewing and Wolf[37] (case 3), Schickele[38] (case 8), Seitz,[39] and Phillips[40] (case 1). The anaesthetic is recorded in only two of these cases (it was chloroform in both), but from the clinical and pathological descriptions and from the date of the publications there can be little doubt that the others are also cases of delayed chloroform poisoning. A similar explanation probably accounts for the centrilobular necroses noted by Ewing (cases 1 and 2), and possibly for the centrilobular degeneration recorded by Drennan and Hicks.[41] Stander also records a case with central necrosis but details of the pathology are not given.

In cases in more recent years in which the anaesthetic was definitely not chloroform the liver contained much fat but did not show any degeneration or necrosis (Saenger, Schjøtt-Rivers cases 2 and 3). Similar appearances of fat in otherwise normal livers are recorded by Heinrichsdorff,[42] Harbitz[43] (cases 9 and 10), Bell (cases 17 and 19), and Schjøtt-Rivers (case 1), but the anaesthetic is not noted in these cases. Two patients dying 4 and 5 days after abortion had multiple focal necroses in the liver, probably of septic origin (Guggisberg; Frankl, case 2).

In the kidneys, catarrhal changes, desquamation, and necrosis of the convoluted tubules are recorded in 9 of the above cases. These findings must again be discounted, as from the descriptions they appear to be only the unrecognized results of post-mortem autolysis. Basal fat in the first convoluted tubules was found in two of the delayed chloroform poisoning cases and in four of the others. Acute pyelitis was present in Tillman's case 1. There was thickening of the glomerular basement membrane in case 19 of Bell.

In the brain, lesions of Wernicke's encephalopathy were recorded in Tillman's case 1 and in de Carle's[44] case 1; there were also some doubtful older lesions of this type in Berkwitz and Lufkin's case 2. These appear to be the same changes as are found in patients before delivery. Retinal haemorrhages were also found by these authors.

Summary.

The pathological lesions found in patients who die of hyperemesis are the results of the vomiting and lack of food.

There is evidence of loss of weight, but the body is usually not greatly emaciated.

The heart is atrophied; the severity of this change is proportionate to the duration of the vomiting.

The kidneys frequently show fat in the mitochondrial zone of the first convoluted tubules; this is dependent on acidosis during the last few days before death, and is not present if there has been adequate administration of glucose during that time.

The liver sometimes shows a fatty infiltration which may be centrilobular or, less commonly, periportal. This appears to be due to mobilization of body fat consequent on starvation.

The brain, in patients who develop the terminal cerebral syndrome, shows the lesions of Wernicke's encephalopathy. Further work is required as to the frequency of occurrence of this important change and as to its exact aetiology, but it appears to be caused by the vomiting and starvation.

Patients who die as a result of vomiting of late pregnancy do not have atrophy of the heart but otherwise show the same changes as in hyperemesis. In addition, they have usually pathological evidence of the aetiological factor, such as pyelitis or hypertensive toxaemia.

Patients who die in the early puerperium after these conditions may continue to show the same lesions that are found in the course of the disease. There may, however, be additional changes due to the anaesthetic or to puerperal sepsis. From the present investigation and from a study of the literature, it seems probable that all the cases of hyperemesis or late vomiting that have been recorded as showing centrilobular necrosis of the liver were really cases of delayed chloroform poisoning. Certain of the other findings reported in the literature, such as necrosis of renal tubules, are only artefacts produced by post-mortem autolysis. The view sometimes put forward, that the liver or kidneys may show any grade of the development of degeneration or necrosis out of the fatty change, does not rest on any satisfactory foundation.

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Some Problems concerning the Aetiology and Treatment of Hyperemesis Gravidarum.*

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THE clinical picture of hyperemesis gravidarum has been known for more than 2,000 years, and yet, in spite of all the advances made by medicine, our knowledge of the cause of this disease and its causal therapy is still at the primitive standpoint, i.e., that the disease is connected with the presence of the ovum in the maternal organism, and that in its most severe form it can be cured only by removal of the ovum. The underlying conditions for its appearance are not known in particular and, consequently, there is no rational conservative causal treatment.

The importance of the problems concerning the aetiology and treatment of hyperemesis may be illustrated by citing some figures: in Denmark, with its population of about 3.7 millions, about 65,000 children are born yearly. According to the statistics for the Lying-in Department A of the Rigshospital, Copenhagen, about 50 per cent of the pregnant women are troubled with vomiting in a more or less severe degree: a slight degree in 24 per cent and a severe degree in 6 per cent, even though it is not pernicious in all the last-mentioned. These figures mean that about 35,000 pregnant women yearly suffer from vomiting, which is severe in 4,200 cases. On going through the archives of the National Health Service for the period of 1931 to 1937, it was found that 40 women had died from vomiting in pregnancy. On application to the respective hospitals, the histories of these fatal cases were obtained and the diagnosis verified. In the same years, 1931 to 1937, according to the compulsory reports to the National Health Service, 224 pregnancies were interrupted on account of vomiting.

* The work here reported was carried out with support from Professor Carl Petersen's Fund.

Among these 224 patients, 17 died in spite of therapeutic abortion.

Thus, in Denmark, vomiting in pregnancy may be said each year to cost the lives of 6 women, to necessitate 30 to 40 therapeutic abortions, and to cause illness and serious inconvenience in over 4,000 women.

Recent investigations on these morbid conditions have been aimed especially to bring to light new pathogenetic factors and, on the basis of such findings, to institute a causal non-operative therapy. Attempt has been made to explain the vomiting as resulting from hormonal insufficiency of the suprarenal cortex, and on the basis of this hypothesis therapeutic experiments were made with suprarenal cortex. Other investigators have thought they were able to demonstrate a change in the production or excretion of gonadotropic hormone, and they have set up these hormonal disturbances as an essential factor in the pathogenesis.

In the following record some modest experiments will be reported to see whether suprarenal cortex, as claimed by American and German authors, is a specific remedy against vomiting. Further, an account will be given of a number of hormonal analyses to ascertain whether the values obtained for gonadotropic hormone in the blood and urine of such patients fall outside the limits for normal variations, and whether the individual patients present any relation between these hormonal values and their clinical features. Finally, I shall try, on the basis of the histories of the forementioned 40 fatal cases, to outline the principle underlying the indicaton for therapeutic abortion in hyperemesis.

The suprarenal cortex theory. It is many years since the hypothesis was advanced that vomiting in pregnancy might be connected with functional failure of the adrenals, and this failure was attributed especially to the adrenal medulla. On the basis of this theory adrenalin therapy was adopted and numerous favourable results were reported. Subsequently, however, it gave much disappointment, and now this therapy has been discarded almost completely. But in recent years the suprarenal insufficiency theory has been revived though now it is no longer adrenalin but the cortical hormone that plays the leading *rôle*. As the evidence in support of the theory of functional insufficiency of the suprarenal cortex, the following observations have been pointed out: (*a*) Hypertrophy of the suprarenal cortex in normal pregnancy, and the assertion that atrophy of this organ is observed in fatal cases of hyperemesis;

(*b*) particular disposition to vomiting in patients with latent, later manifest, Addison's disease; (*c*) clinical and biochemical features of resemblance between hyperemesis and Addison's disease; (*d*) recovery from hyperemesis under treatment with suprarenal cortex.

Here I shall not enter into an estimation of the clinical and pathologic-anatomical basis for the hypothesis of functional insufficiency of the suprarenal cortex, but limit myself to give

The Results of Suprarenal Cortex Therapy in Eleven Cases of Hyperemesis.

The preparation here employed is "corsunal" (Nordisk Insulin Laboratorium), freshly prepared, kept on ice, and tested on epinephrectomized animals. The dosage has been 20 to 30 cubic centimetres injected daily, intramuscularly or intravenously, distributed in 2 to 3 injections, i.e. a dosage similar to that employed in the most severe cases of Addison's disease.

In estimating the effect of a therapeutic agent on vomiting in pregnancy it is to be kept in mind that this illness usually has a tendency to spontaneous recovery, and that it is very often amenable to suggestion, so that the patient not infrequently may be cured by the mere fact of admission to hospital. Therefore, we have never instituted treatment with suprarenal cortex immediately after admission of the patient, but only after she has been under observation for some days and, perhaps, treated with sedatives, sodium chloride, glucose, water, insulin, or ascorbic acid.

Now it turned out that in 5 of these 11 patients there was noticed an improvement in the condition after treatment with suprarenal cortex: the attacks of vomiting became less frequent, the patients were feeling better, and, in particular, the asthenia and anorexia appeared considerably less pronounced. In these 5 patients, however, it is difficult to exclude a suggestive effect. Thus, in three of them some improvement resulted from the admission to hospital. In one case suprarenal cortex was given for several days in large doses without any demonstrable effect whatever; but 7 days after discontinuance of this treatment, spontaneous improvement began and kept on till the patient was well. In 4 patients who were treated energetically, first with glucose, sodium chloride, water, insulin, ascorbic acid and sedatives, and later with large doses of suprarenal cortex, the condition steadily deteriorated, necessitating induced abortion. Only in one case did suprarenal cortex unquestionably

have a favourable effect: this patient had a moderate degree of hyperemesis which was not mitigated by admission to hospital; nor was it improved by sodium chloride, glucose or water. Administration of suprarenal cortex was followed at once by cessation of vomiting and marked improvement of the general condition. After discontinuance of this treatment the vomiting returned. The patient was now told that the suprarenal cortex therapy would again be instituted: but, instead of this remedy, she was given physiologic salt solution in doses similar to the suprarenal cortex injections. This treatment did not have any effect, whereas the patient completely recovered after resumption of the suprarenal cortex therapy.

Thus we have demonstrated, for one thing, improvement of hyperemesis after administration of suprarenal cortex, even though we are not able with certainty to exclude the possibility that the effect in some patients may have been suggestive. On the other hand, it is established that suprarenal cortex is not a specific remedy against hyperemesis. When an effect is obtained, it seems reasonable to look upon it as palliative and compensatory through increase in the liver glycogen and blood-cholesterol, that is, a therapy along the line of the glucose-insulin therapy.

In recent years a number of investigators has reported changes in the aspects of gonadotropic hormones as an essential factor in hyperemesis. Most of the reported analytical results, however, have been obtained in single analyses, and many of these have been compared with Zondek's original curve for prolan excretion, which later had to be revised. Several investigators (e.g., Evans, Browne & Venning, Bjergaard) have found the values for gonadotropic hormone excretion in normal pregnancy to be extremely variable and often very high; and Engle thinks it is very questionable whether it may be possible at all to establish any difference between normal and pathological pregnancy.

The material examined in this respect comprises blood and urine from 6 patients admitted for hyperemesis. The urine was collected and examined throughout the patients' stay in the hospital, and it was assayed for gonadotropic hormone and oestrone. The blood was examined for gonadotropic hormone twice a week. A total of 44 hormone analyses were carried out, each of which was performed on the collective output of urine for 3 days. The values obtained in this way are divided by 3, giving the figures recorded here; these figures, therefore, give

the daily output of gonadotropic hormone in the urine. The 43 analyses made thus represented a total period of 129 days. In addition, as mentioned, the blood of these patients was analysed twice weekly for gonadotropic hormone, 50 c.c. of blood being taken for each assay: 30 analyses of this kind were carried out.

In 4 of these patients the hypermesis was of moderate degree, worse on admission to the hospital, and subsiding gradually till the patients were feeling well at their discharge. In one case, likewise of moderate degree, the patient did not get better, and she was tentatively discharged; but she entered the hospital again, 3 days later, and then her condition was so bad that the gestation had to be interrupted at once, leaving no time for a hormonal analysis covering this period. Finally, one of these patients was admitted to the hospital for hyperemesis, but she was perfectly free from symptoms in the hospital, so that the hormonal analysis in her case can serve merely as a control.

The first question to arise is whether the values obtained for gonadotropic hormone show any deviation from values obtained with the analytical method in normal pregnancy. The answer will be that among the 43 analyses in the 5 cases of hyperemesis the highest value was 513,000 R.U., the lowest 9,000 R.U., and these values fall within the limits for normal variations in perfectly symptom-free gravidae in the corresponding months of pregnancy. It would be of no use to calculate an average value, as the variations are so great.

The next question is, when we follow the curve for urinary excretion of gonadotropic hormone throughout the period of observation in each individual case, do we then find any parallelism between the excretion of gonadotropic hormone and the clinical features of the case?

On critical study of the case-histories and the hormonal values obtained, it is found that even though some of the patients show an increase in the hormonal values concurrent with an aggravation of their condition, and a fall in the values coincident with clinical improvement, there are too many exceptions from this rule to allow of any definite conclusions. Thus in one case there was a rise in the hormonal titre from 23,000 to 324,000 R.U. without any particular change in the degree of hyperemesis. Upon the whole, these patients may be said to show a tendency to higher titre of gonadotropic hormone when they enter the hospital than at their discharge. But this difference is hardly statistically certain and, further, it must be kept in mind

that the curve for excretion of gonadotropic hormone in the urine normally shows a tendency to fall off in the 2nd, 3rd and 4th months of pregnancy.

The concentration of gonadotropic hormone in the blood was found to vary from 200,000 to 1,000,000 R.U. per litre. But in no less than 21 of the 30 analyses did it fall within the limits of 400,000 to 600,000 R.U. These findings show the peculiar fact that the gonadotropic hormone concentration of the blood keeps surprisingly constant, in contradistinction to the hormonal titre of the urine, which shows great and apparently capricious variations.

It has to be emphasized, therefore, that in our cases of moderate hyperemesis, four of the patients recovered, while one was aggravated so as to require therapeutic abortion, the urinary output of gonadotropic hormone was not found to fall outside the range of normal variations. Great and partly unexplainable variations were found in the values here obtained. Also the gonadotropic hormone content falls within the normal limits; in particular, excessively high values were not found even in the worst periods of the more severe cases.

This is partly in conflict with the findings reported by previous investigators, e.g. Anker and Laland, Anselmino and Hoffmann, Brindeau, and Hinglais, and may be attributed, perhaps, in part to the fact that some of those investigations were single analyses or analyses covering merely a short period; besides, the values obtained by some of the authors were compared with Zondek's original normal values, which later were found to be too low. Finally, the previous investigators can hardly have realized how greatly the normal prolan excretion curve may vary, as demonstrated by Bjergaard, Evans, Venning and Browne.

It has to be pointed out, however, that with one exception the cases reported here have been benign. It will be of interest, therefore, to have additional analyses made, especially on malignant cases, in order to ascertain the hormonal aspects of the pernicious cases and see whether they turn out differently. Brindeau has ventilated the possibility that the pernicious cases of hyperemesis might be due to pathological changes in the chorionic villi, and that they might be diagnosed earlier through hormonal analysis. The findings in the worst of our cases contradict such a hormonal diagnosis; but we have not investigated whether the chorionic villi in severe cases present any particular pathological changes.

Still, our material of fatal cases includes two histories of particular interest in this connexion. One of these differs from all the remaining material in the duration of illness. In this case the patient died 14 days after the onset of hyperemesis, while in all the other patients the disease lasted at least one month, mostly over 6 weeks. But in this particular case there was found to be a hydatidiform mole, that is, chorionic tissue undergoing pathological changes.

In the other fatal case the pregnancy was interrupted by therapeutic abortion. After interruption of pregnancy on account of hyperemesis usually one of two things happens: either death within a few days at the most, or cessation of vomiting with complete recovery in 2 weeks at the most. In this patient, however the vomiting persisted for 26 days after the interruption of pregnancy, and then she died. Autopsy revealed retention of a placental fragment.

These two cases call attention to the placenta, the most important endocrine gland in pregnancy, as the possible producer of this disease, and indicate a continuation of the studies on the hormonal aspects of the organism in hyperemesis. Also the excretion of folliculin, which in our analyses did not show any features worth mentioning, ought to be looked into more extensively. Finally, pregnandiol, the corpus luteum product excreted in the urine, as demonstrated by Henry, Venning and Browne, ought to be investigated further with a view to determining its excretion in patients suffering from hyperemesis.

As in hyperemesis the functional insufficiency of the suprarenal cortex and the presence of hyperprolanaemia and hyperprolanuria have yet to be considered hypothetical, we may sum up our present knowledge of the pathogenesis of hyperemesis as follows: owing to some unknown cause, the woman begins to vomit. The further course of the illness may depend to a large extent on psychic factors. A state of inanition develops, of which want of glycogen in the liver is probably the most serious feature, even though the want of salt, water and vitamins, together with the development of acidosis, are also important factors. A specific toxin of hyperemesis has never been demonstrated as a cause of the necrotic changes in the liver and other organs, and it is not inconceivable that these changes may develop as a result of the inanition under the special hormonal conditions present in pregnancy.

Treatment of hyperemesis. In keeping with our view of the

pathogenesis of this disease, the treatment will consist in a psychic, sedative and restorative therapy aimed to counteract the vomiting and its consequences by conservative means; if this is found inadequate, the pregnancy has to be interrupted. The psychic therapy, which often is sufficient in mild cases, consists in a firm suggestive management on the part of the physician, and admission to hospital, possibly with isolation of the patient from the family and from other patients. Sedatives, such as bromides and barbituric acid, have a calming effect on the mind of the patient and lower the irritability of the centre for vomiting.

The restorative therapy consists in administration of glucose, insulin, sodium chloride, water and vitamins. The future will show whether suprarenal cortex is to be established as an effective remedy in the restorative therapy. In severe cases the mentioned substances are given in enemata or by parenteral injection, while nothing is given by mouth.

If conservative treatment on these principles, which are acknowledged everywhere, fails to lead to recovery, it may be necessary to induce abortion, and here we meet with the most important question in th treatment of hyperemesis, namely, the

Indications for Interruption of Pregnancy in Hyperemesis.

Seven symptoms are considered important in this respect: elevation of the temperature above 38°C. (100.6°F.) or persistent subfebrile temperature, persistent increase in the pulse-rate over 100 a minute, jaundice, albuminuria, polyneuritis, ocular symptoms, and psychotic changes. In recent years efforts have been made, but in vain, to find some biochemical test that would be of particular value in deciding to induce therapeutic abortion. Experiments have been made, for instance, with quantitative estimation of chlorine, ketone-bodies and urea in the blood and urine, rest nitrogen in the blood, and quantitative determination of bilirubin in the serum. The bilirubin test is of some value, as it implies the possibility of an early diagnosis of damage to the liver. But the same applies to this test as to various other functional liver tests: none of them are dependable for judging the proper point of time for therapeutic abortion, so that the chief importance is still to be attached to observation of the clinical symptoms.

It is a difficult thing, however, to estimate the significance of the presence, or absence, of symptoms of serious hyperemesis, as is evident from the fact that death from this disease occasionally occurs. In the following I shall try to give a modest contri-

bution to the question concerning the indications for interruption of pregnancy in hyperemesis, as based on

Observations on the symptomatology and judgment of indications for therapeutic abortion in 40 fatal cases of hyperemesis. All the patients were admitted to hospital, even though a few of them did not enter the hospital till immediately before death. The treatment, as a rule, consisted in the aforementioned restorative and sedative treatment, besides therapeutic abortion in 30 of the 40 cases.

In 39 cases the *duration of illness* was more than one month; but in one case the patient died 2 weeks after onset (hydatidiform mole). *Elevation of the temperature* was observed in 27 of 35 cases (no data on the temperature in 5 cases); 14 were subfebrile, 13 had a terminal rise in temperature. *Increase in pulse-rate.* In 13 of 22 patients a pulse-rate over 100 per minute lasted more than 8 days. *Loss of weight* was found in most of the cases, averaging about 1 kg. per week (maximum, 8 kg. in 3 weeks). *Jaundice* was noticed in 22 of the 40 patients; quantitative determination of bilirubin in the blood was made but seldom. *Albuminuria* was observed only in 12 of 38 cases; it was of a slight degree in several cases, and in 6 it lasted less than 3 days. *Psychic symptoms,* such as stupor, haziness, delirium, were recorded in 21 cases, but mostly only a few days before death, although in one patient they were present for 10 days. *Examination of the eyes* was performed only in a minority of the cases; retinal haemorrhages were found in 2, nystagmus in 3, complaints of dimness of vision in 4. *Neuritis* of the extremities was recorded in 2 cases; haemorrhagic diathesis in 1.

From the cases here recorded, it is evident, for one thing, that absence of one or more of the above-mentioned serious symptoms by no means justifies a good prognosis: subfebrile temperature, increase in pulse-rate and jaundice are found in many of these patients, but not at all constantly. Albuminuria is a relatively infrequent and late symptom; severe psychotic disturbances do not usually appear until very late in the course of the disease, when they are common. Ocular symptoms and neuritis are rare phenomena.

On the other hand, the material shows that 25 of these 40 patients presented one or more of the aforementioned serious symptoms for more than one week prior to interruption of pregnancy or death. So the mere presence of one serious symptom has to be taken as a warning.

But is it necessary, then, to interrupt pregnancy in every patient who merely presents one of the symptoms mentioned here?

To elucidate this question we may take the material of patients with hyperemesis who were admitted to the Lying-in Departments A and B of the Rigshospital in the period from 1927 to 1937. This material comprises 74 cases of hyperemesis, 67 of which recovered in response to conservative treatment. Among these 67 conservatively cured patients, 26 presented one or more of the serious symptoms when they entered the hospital. But in all these 26 patients the clinical improvement commenced soon after the admission, and it kept on steadily. All told, then, we have to draw the conclusion that the presence of one or more of the serious symptoms is an indication for interruption of pregnancy if it appears while the patient is under adequate treatment, or if the symptom is present before the institution of treatment and fails to yield to the treatment within a few days.

In 15 of the fatal cases no mention was made of these serious symptoms in the records. On going through the case-histories, however, it is found that in most of these 15 patients the disease had been present for a long time and in a marked degree, in spite of energetic conservative treatment. Our observations, then, emphasize the great importance of the particular indication which Francis J. Browne expresses as "no improvement in a severe case after a week or less under treatment".

The lines, I think, along which we ought to try to solve the problem concerning the treatment of hyperemesis are, firstly, through further biochemical and hormonal investigations to extend our present knowledge of the aetiology and pathogenesis of the disease, and in this way increase the possibility of finding a conservative causal therapy. Secondly, through more close clinical observation to endeavour to arrive at a definition of the indications for therapeutic abortion, by which death from hyperemesis gravidarum may be avoided without sacrificing more foetal lives than necessary.

In conclusion, I wish to acknowledge my indebtedness to Dr. Frandsen, Director of the National Health Service, for access to the archives of the service; to Dr. Pedersen-Bjergaard, Biological Laboratory of Lövens kemiske Fabrik, for the hormone analyses; to Dr. Hagedorn, Nordisk Insulin Laboratorium, for the preparations of suprarenal cortex; and to Professors Dr. Hauch and Dr. Rydberg for permission to make use of the case records of their respective departments.

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Vaginal Implantations in Uterine Carcinoma *

BY

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THE methods by which uterine carcinoma may form secondary or metastatic growths in the vagina, and the clinical implications of such an extension, are matters which perhaps merit more detailed attention than has previously been accorded them.

It is within the knowledge of every gynaecologist that carcinoma of the cervix may extend to a greater or less degree to the adjacent vagina, while the literature tells of the frequency with which secondary nodules of chorion-epithelioma may there be found: but it is not so generally appreciated that carcinoma of the body may also spread in this direction. Again this matter is usually discussed by most writers in a general and rather vague manner, and it appeared that a more exact and detailed study of the pathology of this extension and its significance might be of value.

Apart from the rare cases of primary carcinoma of the vagina, this canal is affected secondarily in three main conditions—carcinoma of the cervix, carcinoma of the body and chorion-epithelioma—and these deserve separate consideration. The involvement is thus always from above, as epithelioma of the vulva practically never involves this canal.

In carcinoma of the cervix vaginal involvement may occur in three ways. Most frequently there is direct spread of the ulceration by continuity to the adjacent vaginal vault and, when the structure of the cervix is destroyed in the later stages, the condition then becomes a carcinoma of the vaginal vault which, however, does not usually extend very far down the vaginal walls.

* A paper read before the eleventh British Congress of Obstetrics and Gynaecology in Edinburgh, April 1939.

The second method is by a non-ulcerative form of extension. This consists of a submucous induration continuous with the cervical carcinoma, and it may extend well down the vagina, so that in advanced cases the canal becomes narrowed with the walls thickened and hard, and in a marked example of this it may be impossible to insert a finger into the vagina.

There can be little doubt but that this submucous extension is by the lymphatics, and it is usually most marked in the anterior vaginal wall.

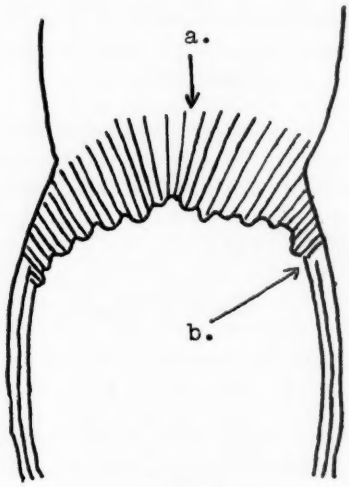

FIG. 1.
This shows the usual direct extension of carcinomatous ulceration from the cervix (a) to the vaginal mucosa (b).

The third type of extension is by discrete secondary growths at an interval from the primary tumour with a varying area of unaffected vaginal mucosa intervening. This may occur in two ways: the secondary growth may be in the upper part of the vagina, and in these cases has been held to be due to simple contact, the so-called kissing or inoculation cancer, or more often it is found in the lower part of the vagina, mostly on the anterior wall and a little behind the orifice of the urethra. Much discussion has centred round this last type of growth, and it has been held by various authors to be due to direct implantation, probably on an abraded surface, to lymphatic spread or to vascular spread.

In a series of 686 cases of carcinoma of the cervix seen in Cardiff Royal Infirmary or privately since 1922 direct ulcerative spread to the vaginal vault (Fig. 1) was present in 354, or 51.6 per cent, and of these 112, or 31.6 per cent, are alive.

The cases with deep submucous infiltration (Fig. 2) numbered 118, or 17 per cent, and of these 31, or 26 per cent, are still living, while 30 cases, or 4.3 per cent, had discrete lower vaginal secondary growths (Fig. 3), and of these 13, or 43.2 per cent, have survived for various periods.

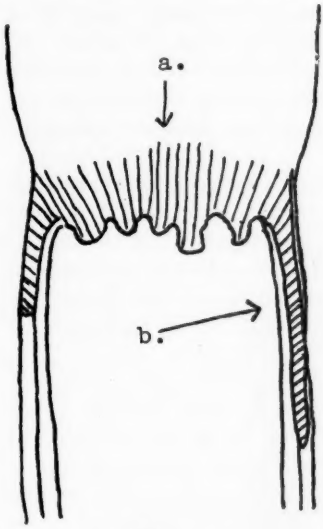

FIG. 2.
To show deep lymphatic infiltration of the vaginal wall (b) from cervical carcinoma (a). Note that in this case there is no ulceration of the vaginal mucosa.

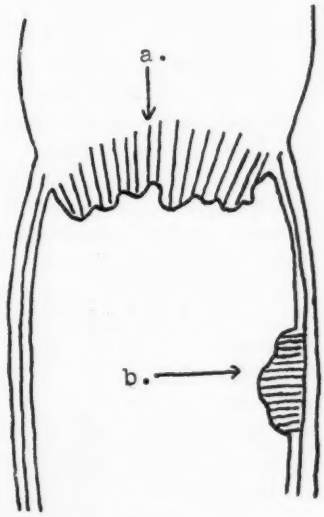

FIG. 3.
This shows the cervical carcinoma (a) confined to the cervix with an inoculation secondary distant growth (b) separated from the parent growth by healthy vaginal wall.

It will thus be seen that out of our 686 cases of carcinoma of the cervix, 502, or 73 per cent, showed vaginal involvement of one kind or another, and the clinical importance of this is evident. When carcinoma of the body is discussed the percentage showing vaginal metastases will be found to be about 13, and clinical experience would lead us to expect some such proportion of incidence.

The most common extension, therefore, is by direct ulcera-

tion, while the least common is the discrete inoculation nodule, with deep lymphatic induration intermediate in frequency.

I have not been able to find comparable clinical statistics for any other large series of cases.

Leitch[1] investigated this condition of vaginal extension in 1922 in an analysis of 847 post-mortem findings, and all will agree with his conclusion that in carcinoma of the cervix the vagina is a very dangerous zone. He found the vagina involved to a varying degree in 97.5 per cent of these cases, but he did not classify the type of involvement.

Leitch favours the lymphatic route as the main method of spread and he dismisses contact transfer, but postulates an occasional separate and distinct vaginal growth due to the same factors as produced the cervical growth, and he supports this by describing certain anaplastic precancerous changes which he has found in the vagina.

The lymphatics of the uterus, cervix, and vagina form a practically continuous meshwork from which the efferent vessels emerge, and it would seem comparatively easy for metastatic cells from the cervix to be carried downwards into the vagina, where they have often been demonstrated deep in the lymphatic spaces. This point has been realized clinically in the extended Wertheim hysterectomy after which recurrence occurs commonly in the vaginal vault, due to the recrudescence of cancer cells buried deep in the lymphatics there, and for this reason the operation has been extended increasingly in the direction of removing more and more of the vagina, and if possible all of it.

Willis[2] agrees with Leitch in rejecting surface implantation from above as the mechanism in the production of discrete lower vaginal growths, and they point out that the necrotic condition of superficial cancer cells likely to be spilled would prevent their growing in another area, while others hold that an abraded surface is necessary for such cells to become implanted. Such an abrasion was not evident at examination, and our clinical observation of such a secondary nodule increasing in size independently of the cervical growth with always an area of intervening normal vagina leads us to the conclusion that such discrete secondaries are produced by implantation of cancer cells which have dropped down from the cervical growth and which have become embedded in the rugae and furrows of the lower vagina until they have taken root here.

In this condition and in a similar condition encountered in some cases of carcinoma of the body to be discussed later the

necrotic state of any spilled cells is really assumed and has never been proven. It would be fair to assume, on the contrary, that some at least of these separated cells are not necrotic and incapable of surviving, and that an occasional clump of such separated cells may be viable and indeed do continue to live and to grow in new surroundings. This would be supported by the fact as shown that such distal implantation occurs in only a small proportion, 4 per cent of cases.

Again, in the operative removal of the uterus for cervical or for corporeal carcinoma an important aspect of the technique is to prevent carcinoma cells being spilled into the operation area by clamping the vagina above the incision, or by suturing the cervix. It does not seem reasonable to assume that in one case the cells are likely to be active and capable of forming recurrent growths, and in the other case necrotic and incapable of so doing.

Vascular extension by the veins would seem to be entirely out of court as a channel for the transference of cancer cells from cervix to vagina, as cervical cancer is known to spread

FIG. 4.
Implantation adeno-carcinoma of the vaginal wall secondary to a primary carcinoma in the body of the uterus. Note the healthy unaffected mucosa between the growth and the cervix. *(From T. S. Cullen.)*

only very rarely by the blood-stream, and in discrete vaginal growths carcinomatous infiltration of the veins has not been demonstrated.

In carcinoma of the body of the uterus secondary vaginal growths are also seen from time to time, but direct surface spread or submucous lymphatic infiltration as seen so often in the cervix is seen only rarely and in cases locally very advanced. The main vaginal involvement is by discrete secondary implants (Fig. 4), again usually in the lower vagina and more often in the anterior wall. In a series of 90 consecutive cases of carcinoma of the body, vaginal implants were present in 12 cases (13.3 per cent), and I have previously reported some of these.[3] None of these patients is now alive.

Of these 12 cases, 6 occurred in patients treated by operation with or without radium, and 6 were in patients treated entirely by radium.

The cases fall into three categories. In the first the vaginal metastases were present when the patient was first seen: this included 5 cases. In the second class were 6 cases in which the vaginal growth was observed only after treatment at intervals of from 3 months to 9 years; while in one case an adenocarcinomatous nodule was found first in the vagina and uterine curettage was negative, but 8 months later the uterus was found to be involved and the spread was rapid.

In the case of corporeal carcinoma direct surface spread to the vagina only rarely occurs, but three other methods have to be considered: there are lymphatic spread and direct surface implantation as with cervical carcinoma, and also vascular metastases, and, in this connexion, it must be remembered that the venous radicles from the corpus, the cervix, and the vagina form at their origin a continuous vascular meshwork very similar to the lymphatic one, with numerous connecting branches, so that it would be comparatively easy for a malignant embolus to be transported in this way. Most observers do not support direct surface implantation, but there are points in its favour, such as the low level of the secondary nodules with intervening healthy mucosa. Again the majority of such patients are multiparae with patulous cervices through which carcinoma cells could easily be extruded, and in such cases a urethrocele or other vaginal fold in which such cells could lie are often present. Again in the course of exploratory curettage or by the manipulation of a uterus during hysterectomy, if the cervix were not previously sutured, such cellular detachment might well

occur, and this would explain the appearance of such nodules after operation.

Schopf[4] in 1891 and Hofmeier[5] in 1895 reported recurrences of carcinoma of the body at the vaginal vault within a year of vaginal hysterectomy, while subsequent perineal wound implantation after a Schuchardt's incision has been reported by Hirsch[6] and Milner[7], and these would all appear to be due to direct spilling of cancer cells at the time of operation.

Cullen,[8] like Leitch, does not favour direct implantation and for the same reasons, but, as mentioned, it does not follow that all cells cast off from the interior of the uterus are necessarily necrotic, especially in the polypoid type of growth when a few cells might well be sufficiently viable to grow on a new soil. Again Ries[9] in a patient with vaginal metastases 18 months after hysterectomy made 500 serial sections of the vagina and could not find any trace of lymphatic involvement. This agrees with one's own clinical experience that at no time during the many repeated examinations of patients with discrete vaginal secondary growths was any lymphatic induration found connecting the primary growth either in cervix or body with the vaginal metastases. In every patient the intervening mucosa remained throughout the entire course of the case normal in appearance and supple on digital examination.

Retrograde lymphatic extension is the mechanism of distant vaginal spread favoured by Cullen and some others, but so far as one knows this has been merely assumed, as a study of the literature does not show any supporting evidence.

In cervical carcinoma, as was shown, lymphatic vaginal extension can be demonstrated clinically by the presence of continuous infiltration, but I do not know of any similar state of affairs that has been shown in the case of the body of the uterus.

Again in carcinoma of the body lymphatic dissemination is not usually marked and occurs only late: much more often cases are found to be inoperable by local extension to the bowel or bladder. Vascular extension by the venous system has been held by some as a possible or probable channel of discrete vaginal implantation. The difficulty in assessing such a means of spread is considerable and has been made more so by the unsupported opinions of many writers who merely state that such an extension is due to lymphatic or vascular spread, but who do not adduce any clinical or experimental evidence to this effect.

Kaufmann[10], however, claims to have demonstrated the lymphatics and veins as the channels of these inoculation metastases

in an accurately studied case. He states, however: "If careful examination proves conclusively that the entire tissue between the main tumour and the metastases is absolutely free of carcinomatous communications, and if a discontinuous deposit of cancer particles by the blood and lymphatic channels is excluded, then the secondary focus may be considered an inoculation metastasis. . . ." But much further investigation is required on this subject.

In chorion-epithelioma vaginal implantation is generally recognized as the most common extension of the growth, but accurate figures regarding its frequency can hardly be obtained as the condition is not common, so that few individual workers can quote a large number of personal cases. Most of the important papers on this subject such as Teacher's[11] and Palmer Finlay's[12] deal with comparatively large numbers collected from the literature, and in many of these the exact occurrence of vaginal secondary implantations has not been noted.

But Pollasson and Violet[13], in a series of 455 collected cases of chorion-epithelioma, found vaginal involvement in 93 cases, 20 per cent, while in Teacher's series of 193 cases, vaginal metastases alone, or with other metastases, were present in 44, about 23 per cent, but in 62 of these cases the record was incomplete or a post-mortem was not recorded, so that the exact proportion with vaginal involvement cannot be known. In general, it would be fair to assume that 20 to 25 per cent would represent the proportion of vaginal involvement in these cases. The special predilection which chorion-epitheliomatous tissue has for vascular penetration is well known, while lymphatic infiltration is practically unknown, and surface spread is seldom extensive. It would, therefore, be expected that secondary deposits in the vagina, as elsewhere, would be due to venous transmission, and this has been shown in many patients by the demonstration of plugs of tumour cells in the uterine and vaginal venous plexuses.

From the above survey it will be seen that in the case of cervical carcinoma extension to the vagina occurs mainly by direct spread of the growth and next in frequency by lymphatic permeation, but that direct inoculation implantation may occur while the vascular system would not appear to be involved in this transmission. In corporeal carcinoma our view is that the usual inoculation metastasis is due to direct surface implantation of cells which have been deposited on the furrows of the lower vagina and which have retained sufficient vitality to grow in this new situation; while in chorion-epithelioma discrete vaginal

secondary implantation is practically always by the vascular stream.

The prognosis in these cases is obviously gravely influenced for the worse by the presence of such secondary vaginal involvement. In the case of cervical carcinoma such cases fall into categories iii or iv of the League of Nations' classification, and the prognostic import of this fact alone is common knowledge. The vagina is a thin walled canal and a carcinomatous growth here rapidly penetrates to adjacent tissues, and in this lies the gravity of the extension. It is very disappointing in a case of otherwise favourable carcinoma of the body of the uterus to find the prognosis reduced practically to zero by the presence of a lower vaginal secondary nodule. Again in cervical carcinoma we have had the experience of seeing the primary growth heal completely with radium, while a lower vaginal secondary deposit did not react well but progressed and later produced a vesico-vaginal fistula and, still later, death.

It would be unfair to draw any conclusions regarding relative prognosis from the figures quoted earlier in this paper, as some of the patients have come under treatment only recently, but it should be noted that in the cases of carcinoma of the body with vaginal inoculation implantation, all have died.

It is more difficult to radiate a vaginal growth than a uterine one, while vaginal carcinoma appears to be in general more resistant to radium than a uterine growth.

The gravity of direct ulcerative spread to the vaginal vault has for long been recognized, and in the days when operative removal was practised more than to-day many of the more conservative gynaecologists considered that this extension alone rendered the case inoperable.

In discussing *treatment* it has to be admitted that we can do very little to prevent the occurrence of such extensions, and in cases of cervical carcinoma the vagina is usually involved before the case is first seen.

In carcinoma of the body, if discrete vaginal secondaries are produced by vascular or lymphatic extension nothing can be done to prevent it except extensive removal of the vagina, which is not usually practised, and suture of the cervix will be of no avail. But if our view is correct that this extension arises from the implantation of extruded cells, then suture of the cervix is of the greatest preventive importance and should always be practised, while vaginal lavage immediately on the completion of operation would be of equal value.

Once such an extension is present the choice of treatment will lie between removal of the vagina and the application of radium, and the first of these represents a formidable addition to hysterectomy in a corporeal cancer, while in cervical cancer too advanced as usual for removal it is out of court.

Radiotherapy is not usually satisfactory in these cases, as the growth does not react well to this therapy or, if it clears up, it soon recurs. The best technique is to bury a sufficient number of long radium needles of 1 or 2 mgm. strength deep to the growth and parallel to the mucosal surface for 72 hours, and to repeat this if necessary according to the reaction. Again if the vaginal growth should be anterior there is danger of a urinary fistula.

The gravity of vaginal secondaries lies in the ease with which they penetrate the vagina so that damage to the rectum or urethra is very apt to occur.

Careful investigation of these points, especially as regards deep infiltration, is thus indicated before the operation is undertaken and it is found that in comparatively few cases will it be indicated. Chorion-epithelioma is the most hopeless and most deceptive type of case in this respect, as the vaginal secondary plum-coloured nodules often appear localized as if they could be enucleated completely and with safety. But they usually return soon and then spread with great speed.

These points have been considered to emphasize the pathological importance of the vagina in uterine malignant disease and the many clinical considerations which also arise.

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The Glycogen Content of the Fallopian Tubes during the Menstrual Cycle and during Pregnancy

BY

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THE discoveries connected with the doctrine of hormones, and in particular the gonadotropic hormones, have explained the numerous relations of the different organs with each other. The effects of the anterior lobe of the pituitary body on the ovary and the connected organs are now generally recognized. We know that the cyclical processes in the mucosa of the uterus are determined by the follicular and luteal hormones. The final object of all these preparatory processes, governed by hormones, is the creation of favourable conditions for the fecundated ovum which is carried through the Fallopian tube to the uterus.

While the operation of the gonadotropic hormone of the anterior lobe of the pituitary body through the ovary on the uterus, vagina and vulva had already been the subject of detailed investigations, its operation in connexion with the Fallopian tube has only been studied during the last few years (Tietze,[1] Caffier,[2] Clauberg,[3] Breipohl[4]). It has been shown that the Fallopian tube also exhibits cyclical phenomena, and that these are hormonally regulated. We distinguish, in the mature woman, two phases corresponding to the transformations of the mucosa of the uterus: (a) the proliferative phase, and (b) the secretory phase of the Fallopian tube. During the proliferative phase, corresponding to the first and second week of the menstrual cycle, the epithelia of the Fallopian tubes exhibit the following features: low ciliated cells, above which unciliated cells project considerably. The unciliated cells are for the most part claviform, and their tapering basis is turned towards the stroma of the Fallopian tube-fold. An irregular level line thus arises. These phenomena correspond to the first week. (Figs. 1*a* and 1*b*). Shortly afterwards, however, the ciliated cells expand into long, slender, palisade cells lying close together, which attain the same height as the unciliated cells.

An almost linear level line thus arises. The unciliated cells become greatly diminished in number, and claviform cells are hardly any longer to be seen. These phenomena correspond to the end of the second week. (Figs. 2*a* and 2*b*). During the secretory phase, corresponding to the third (Figs. 3*a* and 3*b*) and fourth (Fig. 4) weeks of the cycle, a kind of regressive alteration sets in: the ciliated cells become appreciably lower, coarser and barrel-shaped, and their protoplasm at the same time becomes clarified. The unciliated cells now appear in increased numbers, interrupt the rectilinear level line, while they arch their upper end in the direction of the lumen, as if they were about to be expelled. It has never, however, up to now been possible to establish with certainty an actual expulsion of cells into the lumen.

I have recently succeeded, in company with Schäffner, in observing the following characteristic phenomena in a considerable number of normal Fallopian tubes. In the first place, the cyclical changes could be established, in particular in the epithelium, but they never ended in menstrual haemorrhage. They consist solely of two opposing processes. The epithelium is first prepared by a multiplication of high ciliated cells, which partly inure to the benefit of the ovum transporting mechanism. This multiplication continues until shortly before the end of the second week of the cycle. (Fig. 1.) It is accompanied by a germination and multiplication of the vessels of the stroma, which probably serves for the nourishment of ova. From the third (Fig. 2) week of the cycle onwards the enormous wealth of cells in the epithelium is diminished by the expulsion of numerous unciliated cells. A curtailment thus takes place, the object of which is to make room for the necessary sprouting of new cells in the subsequent cyclic phase. The repeated assertion that the epithelium of the Fallopian tube does not menstruate, or that certain processes are to be regarded as substitutes for menstruation, is unnecessary and biologically inaccurate. It would be in the nature of things absurd if the Fallopian tube menstruated, since it serves only for the transport of ova, and also for the nourishment of the ova during transport. It is not the purpose of the Fallopian tube to become an ovum bed, and there will not be any prepared and unutilized ovum-bed to be expelled, in the absence of fecundation, as in the case of the uterus.

New points in our investigations are the ascertainment of the germination of vessels in the fold stroma about the thirteenth to the sixteenth days of the cycle, and, further, the establishment of

the fact that free cells, detached from the epithelium, and also cell nuclei are present in the lumen. More recent investigations, particularly of fibrous cultures (Caffier), have produced proof that the processes above described take place in the Fallopian tube on the artificial introduction of hormones (folliculin, corpus luteum hormones). According to this, the proliferative phase, with its multiplication of ciliated cells, corresponds to the folliculin, and the curtailment of the same, and the appearance of the secretory cells to the corpus-luteum phase.

The principal function of the human Fallopian tube is the transport of the ovum to the uterus. Sobotta[6] and others held that the movements of the tube carry the ovum forward, while Grosser[7] makes the ciliary motion of the epithelia of the tubes responsible therefor. I believe that it is possible, from the investigations now available, to conclude that both mechanisms are operative, all the more that they are under the influence of the same hormone. (Caffier, and Breipohl).

While the histological relations of the Fallopian tube appear now to be largely explained, there are still some obscure points in regard to its histo-chemical relations. The literature on this subject is meagre, and the conclusions contradictory. I have accordingly worked out, on a considerable amount of material in the women's clinic of the university here, the behaviour of glycogen on the human Fallopian tubes during the menstrual cycle and during pregnancy. The behaviour of lipoid will be dealt with in a subsequent study.

Before discussing my own results, I should here like briefly to refer to the most important of the earlier investigations. In 1913 Allister[8] found glycogen in 7 cases out of 25 in the Fallopian tubes of non-pregnant women. In 1916, on the other hand, Tröscher[9] was able to find traces of glycogen only in a few cases in the Fallopian tubes of non-pregnant women, and thought, therefore, that it might be inferred that there was no connexion between the deposit of glycogen and the secretory capacity of the epithelium. In 1927 Jakovlev[10] reported on the glycogen content of the Fallopian tubes of 19 women, including two cases of intra-uterine pregnancy, one complicated by a cyst and the other by a myoma, 4 cases of extra-uterine pregnancy, 1 case of corporeal adenocarcinoma, 5 cases of myoma of the uterus, and 6 cases of ovarian cysts. In the Fallopian tubes histologically examined glycogen was found only in 3 cases. In the one case of intra-uterine pregnancy the glycogen was present in the form of very fine drops in the muscles and connective tissue. In 2 cases of

tubal pregnancy glycogen was found in the decidua (Jakovlev) and in certain villi (the author evidently means chorionic villi) at the place where the Fallopian tube was ruptured. In all the other cases there was no indication of glycogen. In these investigations it is of primary importance to observe that all the Fallopian tubes belong to patients showing subsidiary pathological phenomena in the form of cysts, myomata, or carcinomata. The presence of glycogen occurred in 1 intra-uterine and 2 extra-uterine pregnancies, and even here the glycogen was found only in the stroma and the muscles, in the 2 cases of extra-uterine pregnancy actually in the placenta.

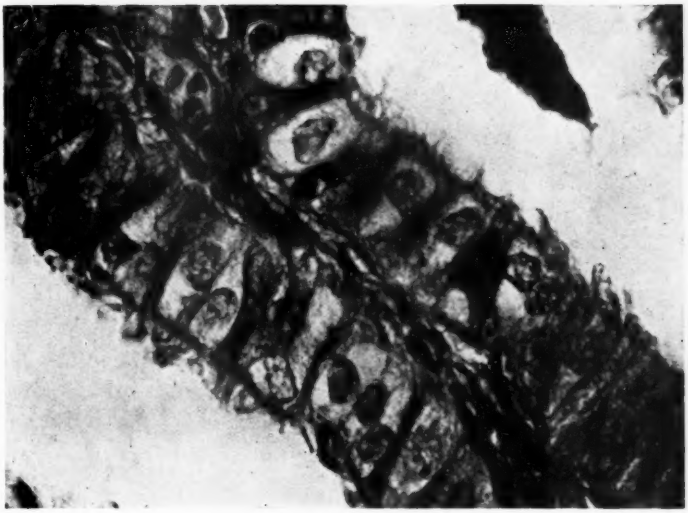
In view of the small amount of material and in the absence of investigations of the Fallopian tubes of normal women the results must be prudently appraised.

In 1929 Iwata[11] published an extensive work on cyclical changes in the Fallopian tube in which he directed attention to the lipoid and glycogen content of the tubes but did not examine any Fallopian tubes of pregnant women. As regards glycogen, he found that this was present in the greatest quantities in all stages of the pre-menstruum, chiefly in the ciliated epithelium. During the time of menstruation, on the other hand, and shortly afterwards, glycogen was not present. Towards the end of the interval there was a gradual increase in glycogen and, as before stated, it was abundant in the pre-menstruum. This study of comparatively healthy material gives results which, for the reasons above stated, cannot be compared with those of Jakovlev.

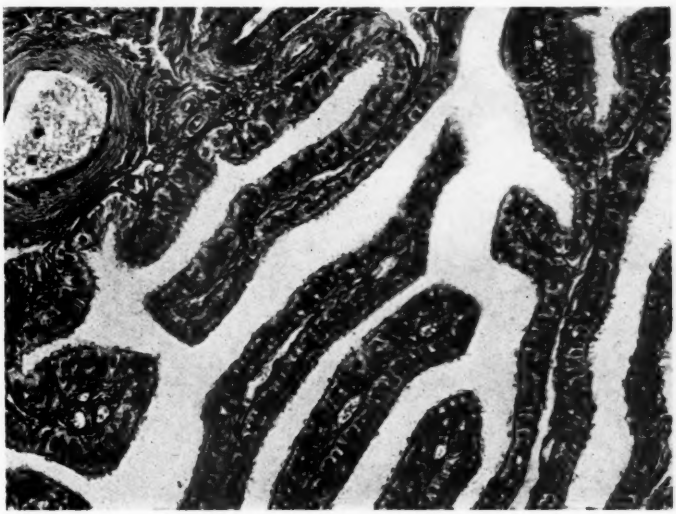
My Own Results

Evidence of Glycogen

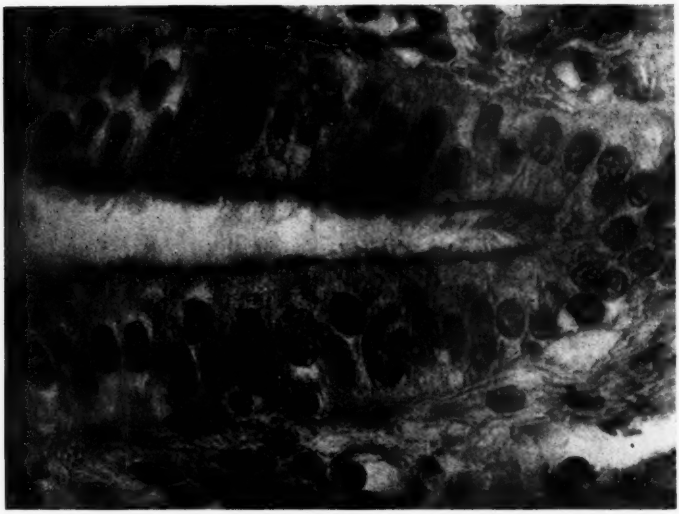
Fallopian tubes during the cycle. Altogether 140 Fallopian tubes were submitted to histological examination, of which 85 were tubes during the cycle and 55 tubes of pregnant women. The material consisted of Fallopian tubes of patients who were operated on in the Women's Clinic of Basle University. In all cases they were tubes of genitally healthy women, who did not show any cyclical anomalies, but who on various indications, mostly psychiatrical, were sent in for sterilization. There were further subjected to examination Fallopian tubes of pregnant women on whom, on similar indications, the Sellheim operation was performed. There were further some Fallopian tubes of the ninth month which were removed in connexion with Caesarean section.



Microphotograph 1(*a*). The proliferative phase to the first (7-day) week of the menstrual cycle.
Haematoxylin: Jaune-solid Wallart. [Large enlargement]

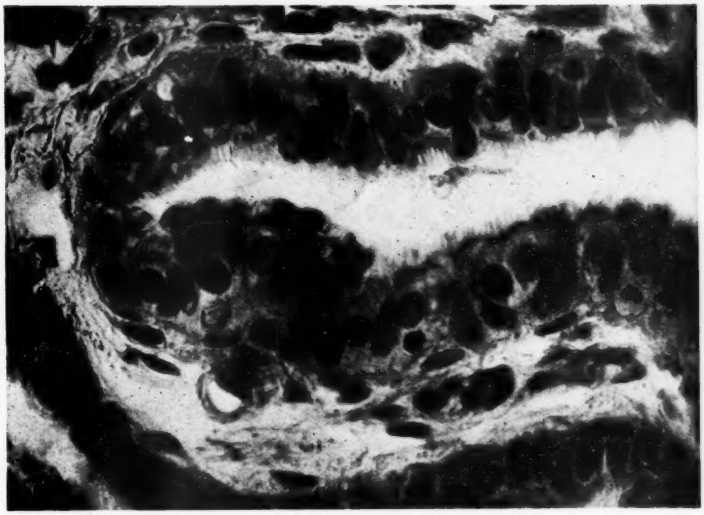


Microphotograph 1(*b*). The proliferative phase to the first (7-day) week of the menstrual cycle.
Haematoxylin: Jaune-solid Wallart. [Small enlargement]

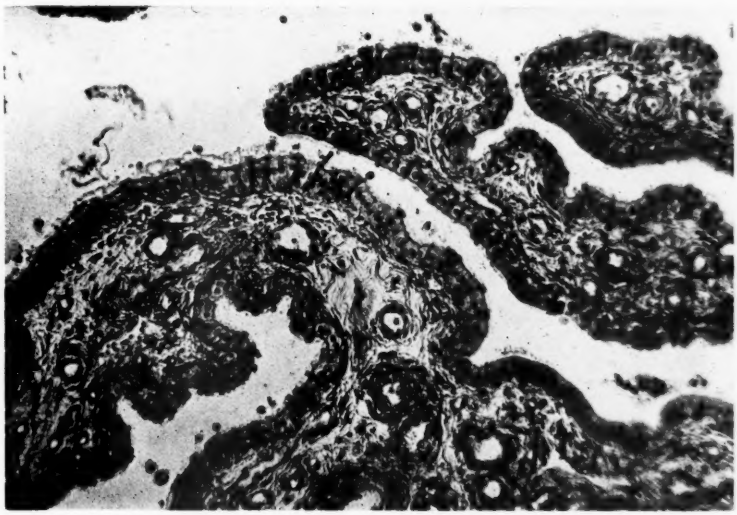


Microphotograph 2(*a*). The proliferative phase corresponding to the second week (10-day) of the menstrual cycle.
Trichrom: Masson. [Large enlargement]

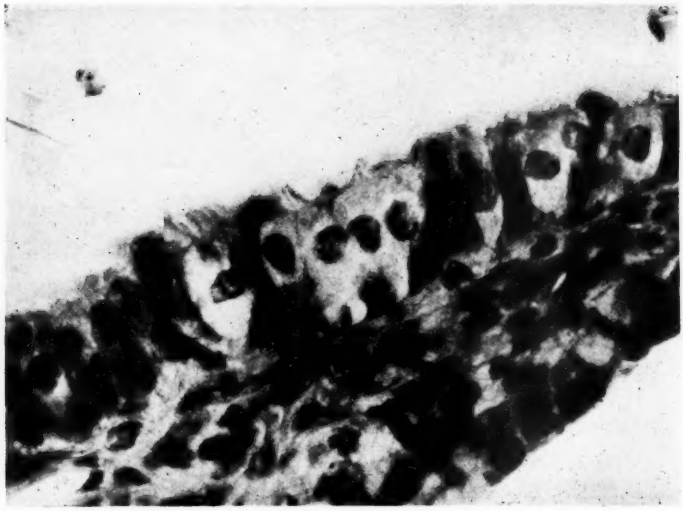
Microphotograph 2(*b*). The proliferative phase corresponding to the second week (10-day) of the menstrual cycle.
Haematoxylin: Jaune-solid Wallart. [Small enlargement]



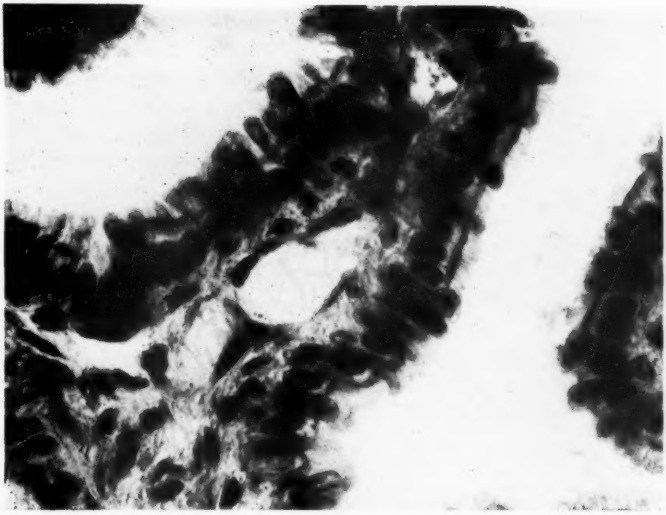
Microphotograph 3(*a*). The secretory phase corresponding to the third week (21-day) of the menstrual cycle.
Trichrom: Masson. [Large enlargement]



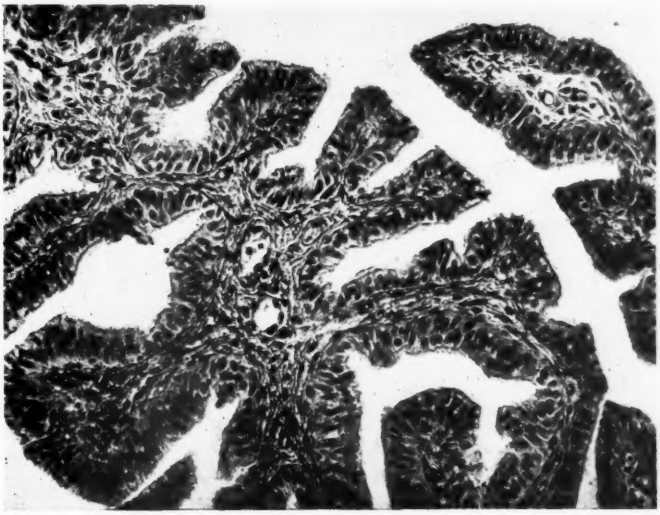
Microphotograph 3(*b*). The secretory phase corresponding to the third week (21-day) of the menstrual cycle.
Haematoxylin: Jaune-solid Wallart. [Small enlargement]



Microphotograph 4. The secretory phase corresponding to the fourth week of the menstrual cycle.
Trichrom: Masson.



Microphotograph 5(*a*). The Fallopian tube of pregnant women resembles the tube of the third to fourth week.
[Large enlargement]



Microphotograph 5(*b*). The Fallopian tube of pregnant women resembles the tube of the third to fourth week.
Trichrom: Masson. [Small enlargement]

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Portions of the tubes were obtained by the subperitoneal resection of a piece of tube 2 centimetres in length (ampullary part), (Labhardt[12]); salpingectomy was also performed when it was desirable to examine the whole Fallopian tube. With a view to obtaining the most perfect possible histological sections the Fallopian tubes after removal were immediately placed in 100 per cent alcohol. Embedding in celloidin was carried out in the usual way. The sections were then coloured with Best's carmine. It is not necessary here to enter into the details of the individual cases; I prefer to set out my results in the following order:

Commencement of the proliferative phase, about the fifth to the eighth days of the cycle.

Later stages of the proliferative phase, about the ninth to the fifteenth days of the cycle.

Secretory phase, about the twenty-second to the twenty-eighth days of the cycle.

Distribution of glycogen: (*a*), epithelium; (*b*), stroma of fold; (*c*), muscular system: internal circular, external longitudinal muscles; (*d*), lumen.

Commencement of proliferative stage, about the fifth to the eighth days, 20 Fallopian tubes were examined. (*a*) In the epithelium glycogen was only sparsely found; similarly very little was present in the stroma of the fold (*b*). On the other hand, somewhat more glycogen, in the form of small grains, was found here and there in the muscular layer (*c*).

In the later stages of the proliferative phase, about the ninth to the fifteenth days, 25 Fallopian tubes were examined. (*a*), In the epithelium glycogen was found in small quantities only in the ciliated cells, never in the unciliated. The deposit of glycogen in the epithelium is quite characteristic, that is to say, it is found in the form of fine grains very near the base of the cell, close to the nucleus. Towards the end of the proliferative stage the glycogen appears to increase.

(*b*) and (*c*). Stroma of the fold and muscular system. Glycogen is found in both tissues, and here also in fine granular distribution.

(*d*) Glycogen is not present in the lumen.

Secretory phase, sixteenth to eighteenth days. In this phase 40 Fallopian tubes were examined.

(*a*) Epithelium. Glycogen was found in the epithelium of all the Fallopian tubes in fine granular form, mostly near the nucleus or around it. Here and there it also lay as a fine granular accumulation under the basal membrane. If this stage is compared with that of the proliferative phase a slight increase of

glycogen in the epithelium may be observed, especially in those which belong to the commencement of the secretory phase. The final stages of the secretory phase rather show a decrease in the glycogen content. The largest accumulations of glycogen were observable about the twenty-second day. (Fig. 3).

(*b*) and (*c*). Stroma of the fold and muscular system. Both show glycogen in the already noted form of fine drops, with the same distribution. The internal circular muscles seem to have somewhat more glycogen than the external longitudinal muscles.

(*d*) Here considerable accumulations of glycogen are also found in the lumen.

Fallopian tubes were not examined at the time of menstruation.

Before proceeding to discuss the glycogen content of the Fallopian tubes of pregnant women, I should like briefly to set out some new results relating to the changes in the mucous membrane of the Fallopian tubes during pregnancy. Very few works exist on the behaviour of the Fallopian tubes during pregnancy (Schmidt,[13] Tietze, Jakovlev, Snyder[14]). When the epithelial changes are compared with those in Fallopian tubes during the menstrual cycle it appears that the Fallopian tubes of pregnant women resemble the Fallopian tubes of the third to the fourth week of the cycle. (Figs. 5*a* and 5*b*.) It is impossible, however, to establish the observance of any definite law. As regards the glycogen distribution in the Fallopian tubes of pregnant women all the 55 tubes examined by me showed the presence of glycogen in all the tissues. Here, too, glycogen is present in large quantities in a fine granular form in the ciliated cells. A visible increase in glycogen could not be established during the various months of pregnancy. The conditions in the Fallopian tubes obtained by Caesarean section in the ninth month are, however, worthy of mention. In 6 cases, in which the indication for Caesarean section arose from a disparity between head and pelvis, the Fallopian tubes showed an accumulation of glycogen, which was perhaps somewhat increased in comparison with the Fallopian tubes during the earlier months of pregnancy. In 2 cases of eclampsia the Fallopian tubes showed very large quantities of glycogen. It is already known that, in cases of eclampsia, the liver, the chief regulator of glycogen metabolism, is seriously affected. We find in eclampsia deposits of glycogen in the most varied organs, and it is, therefore, not surprising that the Fallopian tubes also are very rich in glycogen.

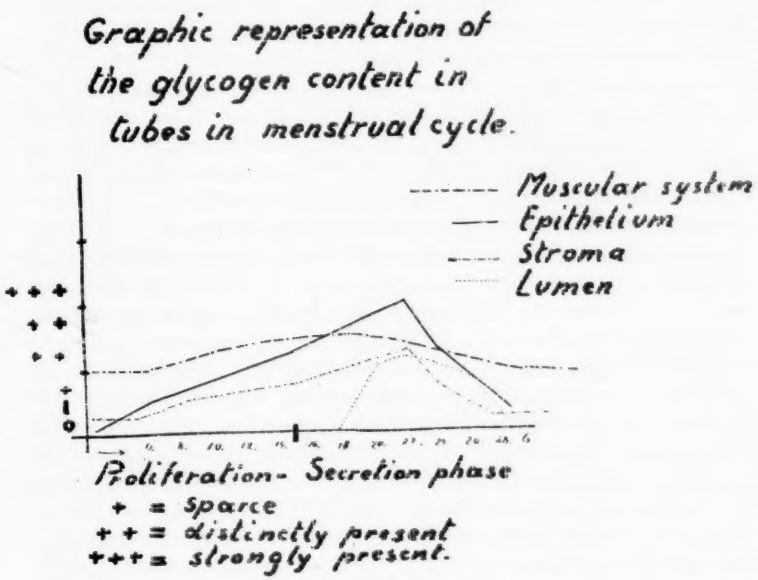

TABLE I.

Summary of Glycogen Results.

One hundred and forty Fallopian tubes were examined for their glycogen content, of which 85 were tubes during the menstrual cycle, and 55 tubes of pregnant women. In all phases, that is to say in the proliferative and secretory stages, glycogen was present. As regards the distribution of the glycogen over (*a*) epithelium, (*b*) stroma of the fold, (*c*) muscular system (internal circular and external longitudinal), (*d*) lumen, it was shown that at the commencement of proliferation, up to about the eighth day, glycogen was met with only here and there, principally in the muscular layer. In the later stages of the proliferative phase, up to about the fifteenth day, it is found in the ciliated epithelia, and also in the stroma of the fold and in the muscular system.

Secretory phase. Glycogen present in all tissues, with a maximal accumulation of glycogen about the twenty-second day of the cycle.

The Fallopian tubes of pregnant women all exhibit glycogen. One tube in a case of eclampsia in the ninth month of pregnancy

showed an especially large quantity of glycogen, which is explained by the generally disturbed glycogen metabolism in eclampsia.

In conclusion, I should like to mention one other interesting tubal condition which I was enabled to observe in a patient of 62 years of age. She was sent to us for operation for an ovarian tumour on the left side. Anamnestically it should be observed that the patient had entered on the menopause at the age of 45, and since that time had not had any haemorrhages or other complications. It was only during the last six weeks that she had noticed that she was becoming increasingly corpulent. At the operation it was found that there was a solid ovarian tumour on the left side about the size of a child's head. The small uterus showed, at its head, two subserous myoma nodules about the size of hazel nuts. The Fallopian tubes were also removed in the operation. The macroscopic and microscopic description of the ovarian tumour is: Pathological Anatomical Institute (Basle), E. No.4040/38: Tumour weighing 850 gr., measuring 14.5 by 12 by 8 cm. On the surface some small cysts, filled with a yellowish fluid, are observable. The tumour is also attached to the ovary. On a large transverse section of the preparation a fibrous tumour of fairly homogeneous appearance is everywhere present. Foreign deposits are not observable. Histologically the large tumour is a fibroma, in part consisting of fine collagenous fibres, and in part showing compact islands of a somewhat more sclerotic character. Epithelial enclosures are not present in the tumour. The tissue in parts shows somewhat more oedematous swelling and is considerably interspersed with vessels. Fibrous bodies are present in the ovary. The vessels in the hilus are strongly sclerotic. The capsule of the ovary is very fibrous. Some cysts on the surface are carried off by the covering epithelium.

On a microscopic examination of the Fallopian tubes, which were fixed and coloured by special methods (see "Dissertation" by Schaffner, Women's Clinic, Basle University), it was found that they corresponded to the secretory phase. We know that the Fallopian tubes of elderly women present quite characteristic features. They have, in fact, the following appearance: simple, finger-shaped, stretching into the lumen, feeble folds without secondary folds; the connective tissue very much enlarged, coarsely fascicular; deficient in elastic fibres, only found here and there in the vascular surroundings. The epithelium is low, cubic, in part quite flat, in a single layer and of uniform appearance, with-

out any ciliated cells. It is known from earlier investigations (Tietze) that the Fallopian tube of the aged resembles that of children, and the Fallopian tube of a mature woman that of the foetus. We find variations from the rule, however, in the Fallopian tubes of elderly women, as the above case shows. Tietze showed in cases of ovarian tumours (material of the Kiel Women's Clinic), in women in the menopause who experienced haemorrhage, that, in 4 cases of granulosa cell tumour and 3 atypical blastomata, the mucosa uteri exhibited a genuine glandular hyperplasia, and the corresponding Fallopian tubes showed a high and highly proliferated epithelium, a functional phase analogous to the endometrium. Another group of secondary and primary ovarian carcinomata showed only a slight stimulation of the endometrium, but the appearance of the Fallopian tubes was absolutely in accordance with the age. Tietze felt bound to infer, with Mayer,[15] Neumann,[16] Schiffmann, Arnold and Körner,[18] that the cause of the phenomena above described was a hormonal influence exercised by the tumour, all the more so that, in a case cited by him, of supposed granulosa cell tumour, quantitative hormone analyses were carried out on the patient by Siebke and Schuschania[19] before and after the operation, and it was found that large quantities of folliculin were excreted before the operation, which disappeared after the operation.

Recently, however, Wallart and Scheidegger,[20] in their work on "*Untersuchungen von Ovarien und verwandten Organen in Alter*", have shown that in old women (e.g., 73 and 77 years of age), with otherwise normal genital organs, the Fallopian tubes showed a hypertrophied and proliferated epithelium. They think that certain functional reasons must be made responsible for this. The authors further conclude that, since the function of the Graafian follicles in dispensing folliculin and lutein ceases at the menopause, in order to explain that part of the phenomena which is determined by hormones, other sources come into force, which arise in the first place from the fibrous bodies constituted by the follicles, supported and stimulated by the rete ovarii and the paraganglionic tissue.

As to my own case, I would only state that in all the beforementioned cases the Fallopian tubes belonged to the proliferative phase, and the glycogen content was in no case examined. In my case the Fallopian tubes showed the changes typical of the secretory phase, and glycogen was present in the Fallopian tubes in all the tissues and also in the lumen.

However, as a result of the latest investigations, it has been

established that the Fallopian tube cycle corresponds to the folliculin and lutein phase and as, moreover, we are in my case concerned with the secretory phase, I feel nevertheless bound to infer a hormonal origin for the changes in the Fallopian tube.

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The Lipoid Content of the Fallopian Tubes during the Menstrual Cycle and during Pregnancy

BY

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IN an earlier study I showed that, as regards the Fallopian tube, the cycle consists of a proliferative and a secretory phase. These cyclical processes are hormonally regulated (Clauberg,[1] Caffier[2]) by the follicular and corpus-luteum hormones. Two important facts were brought out: first, the germination of vessels in the fold stroma from the thirteenth to the sixteenth days of the cycle onwards; secondly, the pressure and expulsion into the lumen of unciliated cells from beginning to end of the secretory phase. It was particularly pointed out that a menstruation of the Fallopian tube, such as some authors assume, does not exist, as this would be an absolutely unbiological process. I was further able to show from a considerable amount of material, consisting of Fallopian tubes of pregnant women, that here the tubes do not change from beginning to end of the pregnancy, but correspond to the secretory phase (about the third week of the cycle). In addition, 140 normal Fallopian tubes of healthy women were examined as regards their glycogen content, including 85 Fallopian tubes during the cycle and 55 Fallopian tubes of pregnant women. In all phases of proliferation and secretion glycogen was shown to be present. As regards the distribution of the glycogen over epithelium, fold stroma, muscular system and lumen, it was shown that, at the beginning of the proliferative phase (end of the first week of the cycle) glycogen is only met with here and there in the muscular stratum and also in the epithelium. Towards the end of the proliferative phase it is distinctly present in the ciliated epithelium and also in the fold stroma and the muscular system. During the secretory phase glycogen is present in all the tissues, with a maximal accumulation of glycogen about the twenty-second day of the cycle. The Fallopian tubes of pregnant women all exhibit glycogen, while a Fallopian tube in a case of eclampsia in the ninth month of pregnancy showed particularly large quantities of gly-

cogen, which was explicable by the generally disturbed glycogen metabolism in eclampsia.

The present study is concerned with the lipoid content of the Fallopian tubes. For this investigation also only normal tubes of genitally healthy women were employed. Before, however, discussing my own results, I should like to briefly refer to the literature on the subject, which is to a great extent contradictory.

The first statements concerning the lipoid content of normal Fallopian tubes date from 1917. Tröscher[3] reported that he had found sudanophil grains in the epithelium of Fallopian tubes; Arndt,[4] on the contrary, in 1919, could not find any trace of lipoid in 25 Fallopian tubes in the inter-menstruum. Investigations were known of a much earlier date regarding the lipoid content of Fallopian tubes affected by inflammatory changes, for example, gonorrhoeal salpingitis or pyosalpinx, in which lipoid was everywhere present (Aschoff,[5] Amersbach,[6] Kawamura,[7] Pick,[8] Orth[9]). In 1926 Scheyer[10] reported on lipoids in Fallopian tubes, on the basis of the examination of 134 tubes taken from corpses and 21 removed in operations. The fresh material was derived from Fallopian tubes at the end of a normal pregnancy, and only 7 tubes were, in his opinion, in a normal condition and obtained at various stages of menstruation. On an examination of all this material Scheyer found lipoid in only 7 cases. In all the others he found lipoid in various quantities in the connective tissue, in the muscles, and also in the tubal epithelium. His results may be summarized as follows:

An active secretion of lipoids by the Fallopian tube epithelium does not exist, and the quantity of the lipoids contained in the Fallopian tubes is directly proportional to the lipoid content of the blood; that is to say, it increases with increasing age, and may also increase in cases of pregnancy, eclampsia, uraemia, and anaemia, in short in all complaints which give rise to a greater or lesser degree of lipaemia. According to Scheyer, lipoids are entirely absent from the Fallopian tubes of new-born infants, and they are only sparsely present in children. Chronic salpingitis in no way influences the lipoid content of the tubes. As regards the importance of the menstrual cycle for the lipoid content of the tubes Scheyer thinks it must be inferred from his 7 cases that the lipoid content is greater before and during menstruation.

In 1927 Butomo[11] published a lengthy work dealing specially with the lipoid content of the Fallopian tubes. He examined 72 normal tubes and 30 tubes affected by inflammation. His results

may be summarized as follows: The presence of morphologically visible lipoids in the Fallopian tubes is to be considered as a physiological phenomenon. The bulk of the tubal lipoids belong to the class of neutral fats. The lipoid content of the tubes diminishes during pregnancy and in the climacteric, even to the point of complete disappearance of fat. The greatest lipoid content is found in the tubes at the height of the inter-menstruum. Parallelism does not exist between the lipoid content of the tubes (neutral fat) and that of the blood (also neutral fat). In the overwhelming majority of normal tubes a certain distribution of lipoids in the epithelium corresponds to a quite definite period of the menstrual cycle. In chronic inflammation of the tubes only the nature and manner of the distribution of the lipoids in the epithelium is disturbed, as compared with normal tubes.

In 1929 Iwata[12] dealt with the lipoids of the Fallopian tube in the course of a larger work on the morphology of the human Fallopian tube. He compared the lipoid content of the tube with that of the uterus, and found that there is a parallelism between the lipoid content of the tube and that of the uterus. He found lipoid in all phases of the cycle, chiefly in the pre-menstruum, but also in the menstruum and the post-menstruum. As regards localization, he found it in the muscular cells, the stroma and the epithelium.

These are briefly the most important works on the lipoid content of the Fallopian tubes. If we submit all these results to a critical study, the difference of opinion among the different authors is striking. Moreover, the results obtained by Scheyer, who examined only 7 normal tubes within the cycle, cannot be compared with those of Butomo, who analysed 72. The labours of Butomo and Iwata, based on extensive, approximately normal material, enlarge our knowledge of the lipoid distribution in the various phases of a woman's life, particularly during the cycle.

My Own Results.

As already mentioned, the Fallopian tubes submitted to examination were normal tubes of genitally healthy women who were sent for sterilization, or for the Sellheim operation, on psychiatric and other indications. In some cases pieces of tubes from the ampullary part were obtained by subperitoneal resection by Labhardt's[13] method, or complete tubes were obtained by salpingectomy. The preparations were immediately placed in 4 per cent formalin, and frozen sections were made after 24 hours. I expressly state after 24 hours, as if the material remains longer in

formalin the fat content disappears. The tubes were then stained with the usual stains.

The fat found was principally neutral fat. I deal with the distribution of the fat in the following manner only for the sake of greater clearness: (*a*) epithelium, (*b*) fold stroma, (*c*) muscular system, (*d*) subserous and intramuscular connective tissue. I was able to demonstrate the presence of lipoid in all the cases investigated by me. Generally speaking, it appears in the form of very fine grains, and also in larger grains, and finally in the form of smaller or larger drops. As regards the distribution of lipoid in the various phases of the cycle, lipoid was found in the first half of the proliferative phase (beginning about the fifth to the sixth days) in the form of very fine grains in the epithelium, more in the form of cohering drops in the fold stroma, and sparsely in the muscular system and the connective tissue. During the second half of the proliferative phase the lipoid is found more dispersed in the epithelium, and also here and there in the muscular strata. It must be pointed out that the examination did not show the same quantity and distribution of lipoid in all tubes of the same day of the cycle; several tubes of the same day of the cycle were examined.

At the beginning of the secretory phase (about the twenty-first day of the cycle) the lipoid content was found in varying quantity in all the tissues in the form of large drops, chiefly in the subserous connective tissue, and also in granular form in the muscular system, sometimes along the nucleus, sometimes apart from it. Lipoid is also found diffusely distributed in the fold stroma. In many preparations the lipoid deposits in the epithelium are also characteristic. It is found almost everywhere in the form of medium-sized and small drops going from the nucleus in the direction of the lumen. The greatest accumulation of lipoid in the tube appears to exist in this phase.

In the second half of the secretory phase we find a slight diminution in the lipoid content, especially in the epithelium, but also in the fold stroma.

I cannot, however, from my investigations, arrive at any law governing the distribution and quantity (Butomo) of lipoid, as I found in the most varied phases of the cycle fluctuating transitions in the distribution and quantity of the lipoid. The impression is produced, however, that in general the greatest lipoid content is found at the beginning of the secretory phase.

As regards the distribution of lipoid during pregnancy, I was able in all the Fallopian tubes examined by me to demonstrate the

presence of lipoid everywhere in varying quantities, particularly in the epithelium. Here also it is difficult to say whether we have a diminution of lipoid with advancing pregnancy (Butomo). Butomo also called attention to the fact that the tubes of old women do not show any lipoid. I have examined altogether 10 Fallopian tubes of elderly women between 58 and 72 years of age as regards their lipoid content, and in every case was able to demonstrate the presence of lipoid, although the Fallopian tubes showed all the histological changes of old tubes and were otherwise absolutely normal.

To sum up briefly, I was able to demonstrate the presence of lipoid in all stages of the cycle, and also during pregnancy and in old age, in varying quantities and distribution.

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Further Investigations on the Induction of Uterine Haemorrhage by means of Progesterone

Second Report

BY

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As recently reported by us in this journal,[1] haemorrhages are produced during the intermenstrual stage in the normally menstruating women by means of parenteral administration of progesterone: intracyclical haemorrhage. If a woman is injected with 10 mg. of progesterone* daily during the post-menstrual stage, i.e. from the fifth to the ninth or from the seventh to the eleventh day of the cycle, a total dosage of 50 mg., haemorrhage sets in after an interval of 60 hours, that is on the twelfth or the fourteenth day of the cycle, and persists for 3 to 4 days. During the period when progesterone is given the patients notice swelling and pain in the breasts, as well as pain in the abdomen, all these symptoms subsiding as soon as the haemorrhage commences. The blood discharged in this intracyclic haemorrhage does not coagulate, a quality characteristic of true menstrual blood.

I. *Progesterone Administration in the Intermenstrual Stage.*

What is the effect of progesterone if injected in the intermenstrual stage, that is at a time when the woman, after follicular rupture, is already under the influence of the progesterone formed endogeneously in the corpus luteum? In our first report we have

* As we have previously reported elsewhere, the same effect can be achieved with the oral administration of pregnen-in-on-ol as is noted with the parenteral administration of progesterone. In a normally menstruating woman we produced intracyclic haemorrhage with 300 milligrams of pregnen-in-on-ol. The same dose produced a haemorrhage in a case of secondary amenorrhoea without any preliminary treatment with oestrogenic hormone.

already described two such cases. In the first case progesterone had been given from the eleventh to the fifteenth days of the cycle, and on the eighteenth day the onset of the haemorrhage was observed during an operation for myoma of the uterus. In the second case the hormone had been injected from the twelfth to the sixteenth day of the cycle. Haemorrhage, however, did not take place precociously before the normal period of menstruation. We treated four other patients in a similar manner, injecting 50 mg. of progesterone in two patients from the eleventh to the fifteenth day, in one from the twelfth to the sixteenth day of the cycle, and in one from the fifteenth to the nineteenth day. (Table I and Fig. 1.) Precocious bleeding could not be produced in any of these patients, and the haemorrhage did not occur before the normal menstrual period. There is, therefore, a characteristic difference in the action of progesterone depending on the cyclic phase in which it is administered. If progesterone is given in the postmenstrual stage the haemorrhage occurs in the intermenstruum; if it is given during the intermenstruum, there is no effect whatsoever. Haemorrhage occurs only if there is an interval between the administration of progesterone and the period when it is formed endogeneously. If the exogeneous administration of progesterone merges with the period of the formation of progesterone in the corpus luteum, there is no haemorrhage.

Subsequent menstruation occurs at the normal term (*cf.* Table I, Cases 1, 3, and 4). The use of progesterone during the second half of the cycle, therefore, does not interfere with the ovarian cycle.

II. *Prevention of the Intracyclic Haemorrhage through Follicular Hormone.*

By administration of 50 mg. of progesterone in the post-menstrual stage a haemorrhage during the intermenstruum is brought about: intracyclic haemorrhage. The oestrone level which is physiologically present during the intermenstrual stage does not prevent the haemorrhage; if, however, additional amounts of oestrogenic hormone are given the inhibitory action becomes effective. In five patients we injected, subsequent to 5 days' treatment with 50 mg. of progesterone (10 milligrams equals 100,000 international units of oestradiolbenzoate) daily for 4 days; the total dose, therefore, amounting to 40 mg. (Fig. 2). The intracyclic haemorrhage which had previously appeared subsequent to progesterone administration after an interval of 60 hours did not occur in any of these patients (*cf.* Table II).

CASE No. 1. Progesterone had been given from the fourth day to the eighth day of the cycle, oestradiolbenzoate from the ninth day to the twelfth day. If progesterone only hade been given the haemorrhage would have occurred on the eleventh day of the cycle. It did not, however, occur before the fifty-second day, and was, therefore, delayed by 41 days. (Fig. 2.)

CASE No. 2. Progesterone had been given from the fifth to the ninth day of the cycle, oestradiolbenzoate from the tenth to the thirteenth days. If progesterone only had been given, we should have expected the onset of the haemorrhage on the twelfth day of the cycle. It occurred, however, on the fifty-third day, and was, therefore, delayed by 41 days. The uterine mucosa, as ascertained by histological examination of a strip, was in the menstrual stage of development.

CASE No. 3. Progesterone had been given from the fifth to the ninth days, oestradiolbenzoate from the tenth to the thirteenth days of the cycle. If progesterone only had been given the haemorrhage would have been expected on the twelfth day. It occurred, however, on the nineteenth day, and was, therefore, delayed by 7 days. Examination of the mucous membrane revealed a pseudo-menstrual bleeding occurring from a proliferative mucosa.

CASE No. 4. Progesterone had been given from the seventh to the eleventh days and oestradiolbenzoate from the twelfth to the fifteenth days of the cycle. If progesterone only had been given bleeding would have been expected on the fourteenth day; it occurred, however, on the forty-fourth day, and was, therefore, delayed by 30 days. Histological examination showed a progestational mucosa, demonstrating, therefore, that we were dealing with a true menstrual haemorrhage.

CASE No. 5. Progesterone had been given from the eighth to the twelfth days, and oestradiolbenzoate from the thirteenth to the sixteenth days of the cycle. If progesterone only had been given we should have expected the onset of the haemorrhage on the fifteenth day. It did not occur, however, before the twenty-fourth day, and was, therefore, delayed by 9 days.

These observations demonstrate that:

1. The intracyclic haemorrhage is prevented by oestrogenic hormone.

2. The duration of this inhibitory action varies from 2 to 41 days. In two of the cases (Nos. 3 and 5) the haemorrhage occurred during the course of the cycle; in three cases (Nos. 1, 2 and 4) it was postponed, thus bringing about artificial amenorrhoea. This observation need not surprise us, since follicular hormone, at least 70,000 m.u., is able to inhibit menstruation (Zondek[2]). The follicular hormone inhibits the secretion of the luteinizing hormone

of the anterior pituitary (prolan B), thus disturbing the development of the corpus luteum. There is, therefore, an insufficient production of progesterone, which in its turn prevents the progestational transformation of the uterine mucosa. Protracted treatment with large doses of hormone (60 mg. of oestradiolbenzoate during 60 days) results in hormonal sterilization of women, and, without the formation of corpus luteum the ovaries appear like those of an old woman (Zondek[3]). The oestrogenic hormone, consequently, can bring about:

(a) inhibition of the haemorrhage-producing action of progesterone;

(b) inhibition of the gonadotropic secretion of the anterior pituitary.

Summary.

1. Progesterone, if administered during the post-menstrual stage, induces intermenstrual haemorrhages in the normally menstruating woman: intracyclic haemorrhage.

2. Progesterone is not effective if given in the intermenstrual stage, i.e. during, or subsequent to the rupture of the follicle, at a time, therefore, when the woman is already under the influence of the endogeneously produced corpus luteum hormone. The intracyclic haemorrhage, therefore, does not occur if there is not an interval between the exogeneous administration and the endogeneous production of the corpus luteum hormone.

3. The oestrone level which is physiologically present during the intermenstrual stage does not prevent the intracyclic haemorrhage; if, however, additional amounts of oestrogenic hormone are given the inhibitory action becomes effective. The oestrogenic hormone interferes with the haemorrhage-producing effect of the corpus luteum hormone, as well as with the gonadotropic mechanism of the anterior pituitary.

4. Pregnen-in-on-ol given *per os* has the same effect as has progesterone given parenterally.

Progesterone, progestine, and oestradiolbenzoate (dimenformone) were kindly supplied to us by N. V. Organon Oss.

TABLE I.

Progesterone administration in the inter-menstruum.

	No. 1 J.	No. 2 M.	No. 3 K.	No. 4 M.
Progesterone treatment day of the cycle ...	11 to 15	11 to 15	12 to 16	15 to 19
Bleeding: day of the cycle ...	26 to 30	27 to 29	28 to 31	25 to 27
Following bleeding: day of the cycle ...	54	—	55	49
Interval between the two haemorrhages	28	—	27	24

TABLE II.

Inhibition of the intracyclic haemorrhage through follicular hormone.

	No. 1 K.	No. 2 N.	No. 3 J.	No. 4 N.	No. 5 N.
50 mg. of progesterone, day of the cycle	4 to 8	5 to 9	5 to 9	7 to 11	8 to 12
40 mg. oestradiolbenzoate, day of the cycle	9 to 12	10 to 13	10 to 13	12 to 15	13 to 16
Haemorrhage, day of the cycle	52 to 55	53 to 56	19 to 22	44 to 47	24 to 30
Uterine mucosa	—	Mens.	Psuedo-menstrual	Mens.	—
Inhibition through oestradiol-benzoate, in days	41	41	7	30	9
Following haemorrhage, days after	24	30	30	—	—

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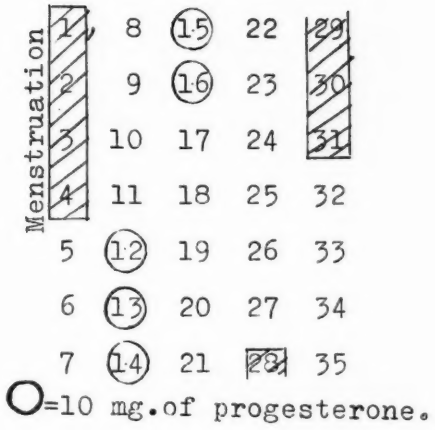
Menstruation
1 8 15 22 29
2 9 16 23 30
3 10 17 24 31
4 11 18 25 32
5 12 19 26 33
6 13 20 27 34
7 14 21 28 35
=10 mg.of progesterone.

FIG. 1.

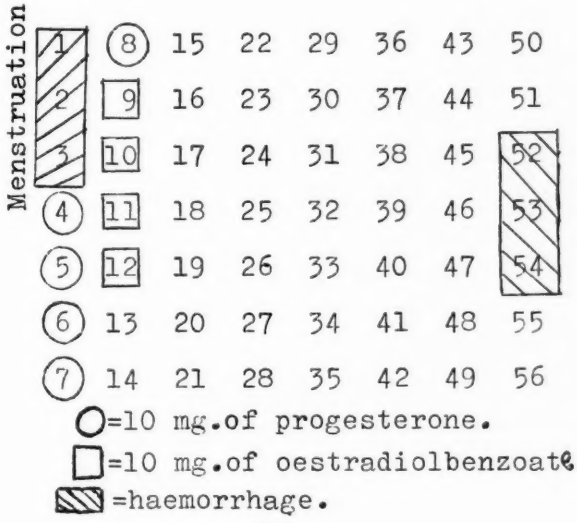
Menstruation
1 8 15 22 29 36 43 50
2 9 16 23 30 37 44 51
3 10 17 24 31 38 45 52
4 11 18 25 32 39 46 53
5 12 19 26 33 40 47 54
6 13 20 27 34 41 48 55
7 14 21 28 35 42 49 56
=10 mg.of progesterone.
=10 mg.of oestradiolbenzoat
=haemorrhage.

FIG. 2.

The Effects of Emotional Stress on the Contractions of the Human Uterus.

Preliminary Report.

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INTRODUCTION.

THIS report deals with certain aspects of the motility of the human uterus, and the *data* presented have been collected in the course of an investigation into the cause of primary dysmenorrhoea.

The uterine muscle, being plain muscle, possesses inherent rhythmic activity common to all plain muscle, and its fundamental reactions depend upon the nature of this type of muscle and also on the form which it takes, which is that of a hollow muscular organ.

Normal contractility depends upon many factors such as normal development of the body and the cervix, normal hormonal sensitization, normal distribution of the double nerve supply and normal endometrial structure. The emotions, too, apparently play a part.

Abnormal contractions of the uterus in certain conditions give rise to pain and, as is the view now widely held, the pain and discomfort of primary dysmenorrhoea are, in many cases, due to disordered action of the uterine muscle.

In the treatment of dysmenorrhoea one or more of the above factors may be considered to be abnormal and treatment is directed accordingly: controlling or regulating uterine muscular action is very frequently the aim of treatment.

It is well known that in the experimental animal the ovarian hormones have a profound effect on the motility of the uterus.

The hormones oestrone and progesterone are antagonistic; under the influence of the former the rate and amplitude of the contractions are increased, while the response of the uterus to the latter is a decrease in activity. In the rabbit prior to ovulation posterior pituitary extract causes greatly increased contractions; in the presence of a corpus luteum in the ovary, however, a reaction is not observed. Reynolds[1] demonstrated these reactions in the rabbit, using an intra-uterine hydrostatic bag connected to a manometer which recorded changes in the volume of the fluid in the bag. Knaus,[2] using an apparatus similar in principle, obtained similar results in the human female, but the observations of other investigators have been found to be contrary to those of Knaus, especially in respect of the reactions of the uterus to posterior pituitary extract in the secretory phase of the cycle. It is now generally accepted that the human uterus remains actively contracting throughout the two phases of the menstrual cycle and that the contractions of the uterus are even greater in the second half of the cycle than in the first half. The uterine contractions during the process of menstruation are many times stronger, as measured by the hydrostatic bag method, than those recorded during the proliferative and secretory phases. Posterior pituitary extract causes spasm of the uterus and an increase in the contractions throughout each phase of the menstrual cycle.

It will be seen, therefore, that the reactions of the uterine muscle have been already widely studied from many aspects, but one aspect of this activity which, so far, has received little attention is the reaction of the uterus to emotional stress. Psychogenic control of uterine contraction and associated pain may play a very important *rôle* in dysmenorrhoea. That this seems to be the case is shown, for example, when the most trivial happening may quite suddenly cure severe dysmenorrhoea; on the other hand, it is well known that the most extensive and elaborate treatment may be entirely without obvious effect in a certain type of patient.

A review of the literature fails to reveal any mention of observations on the effect of emotional stress on the contractility of the uterus. While nothing definite regarding the cause of dysmenorrhoea has emerged from this investigation so far, a report of some direct evidence of the effect of emotional stimulus on the uterus may be of interest at present. Later, when this work has proceeded further, it is hoped that other uterine reactions will be discovered which will aid in elucidating the

aetiology of primary dysmenorrhoea and in providing a basis for effecting curative treatment.

The Investigation.

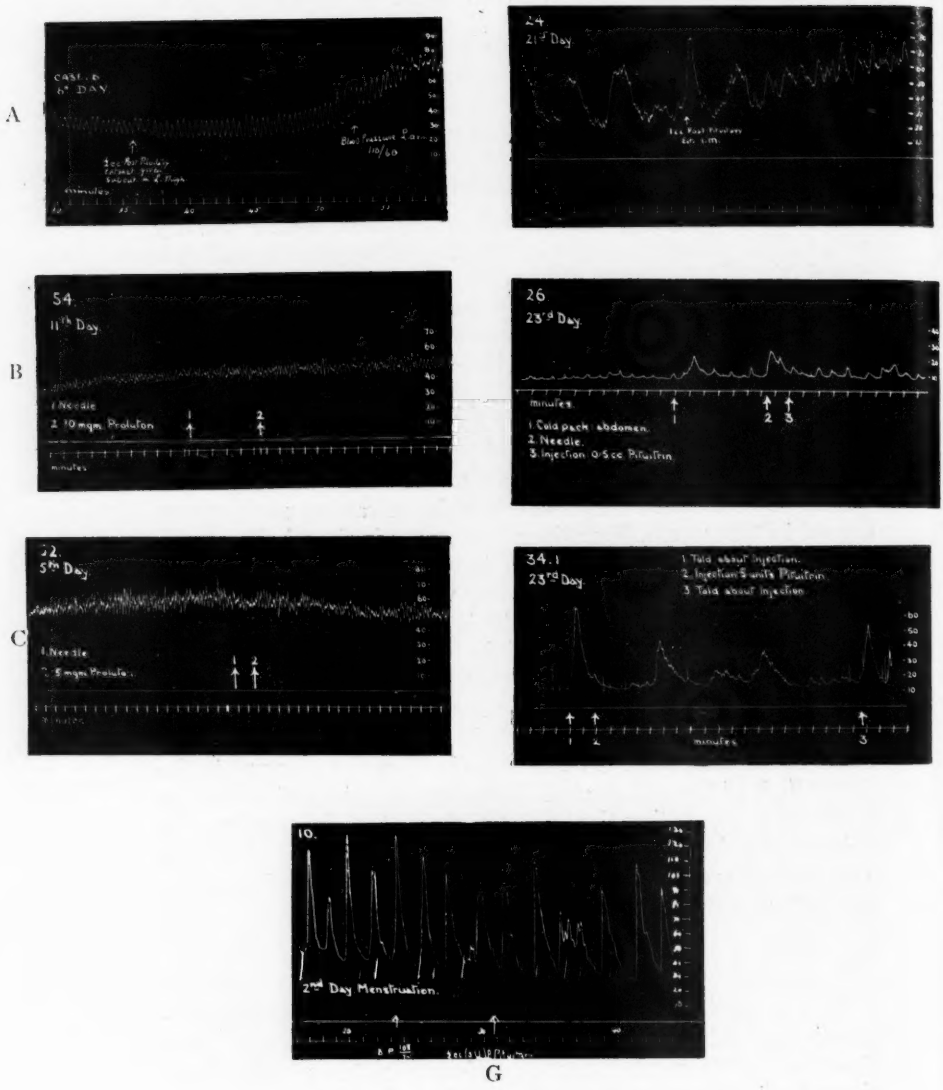
Technique.

In this investigation the method of recording uterine activity was similar to that employed by Moir.[3] The apparatus used consisted of an intra-uterine hydrostatic bag connected by pressure tubing to one limb of a mercury manometer. Water filled the system from the bag to the manometer. A float in the free limb of the manometer carried a writing point which recorded on a smoked drum. A T-piece glass tube was inserted at one point in the length of the pressure tubing and through this side-piece water could be injected into the system with a 1 c.c. syringe. The manometer acted as a means of transmitting to the writing lever the fluid surges which each contraction of the uterus caused in the system. Variations in pressure in the whole system, which included the small bag in the uterus, were similarly recorded by the manometer. The bag was introduced, collapsed, into the uterine cavity at the beginning of each observation, and then 2 to 3 c.c. of water were injected through the side-piece, which was then closed. As only pressure tubing was used in the system, most of this extra fluid caused fluid to enter the bag, which was made of the thinnest rubber and so easily dilatable. Some of the fluid went to depress the level of the mercury in the closed limb of the manometer. Knowing the calibre of the manometer tube and noting the extent of the fall of the mercury the volume of fluid which had entered the bag could be calculated. The average pressure in the system after the addition of the extra fluid to the system was 45 mm. mercury.

Procedure.

In this particular study 30 patients were examined, all comparatively healthy women. In no patient was there any gross abnormality of the pelvic organs. Fifteen minutes to half an hour elapsed after introduction of the bag into the uterus before the tracings recorded were made. After each record had been completed a biopsy specimen of the endometrium was taken with a special tubular curette.

After it was seen on the recording drum that a fairly constant record was being produced, the patient was told that she was



RECORD OF CONTRACTIONS OF THE HUMAN UTERUS.

On the right pressure in millimetres mercury. Time in minutes.

A, B, C Proliferative phase: no response to emotional stimuli.

D, E, F Secretory phase: response by increased contraction to emotional stimuli.

G Menstruation phase.

about to receive an injection, and after the area of the skin had been suitably prepared the injection was administered. When this information was received by some patients the writing point on the drum was seen to rise quickly, indicating thereby a reactionary contraction of the uterus. In others this reaction was slightly delayed until the needle was actually pricking the skin. In some cases posterior pituitary extract was being given, but that this was not the cause of the contraction was proved when an inert fluid was injected with a positive effect on the uterus, or when a cold pack was laid on the abdomen as a stimulus, or when the only stimulus was the noise of a tin basin being dropped into a pail on the floor.

Results.

An analysis of the results is given in the "Table of Results" and specimen tracings taken from the collection which has accrued during the investigation are shown in the "Contraction Records".

In this group of 30 cases, 10 were in the proliferative phase when examined by this method, and 20 were in the secretory phase. According to the results obtained in this series, an emotional stimulus applied in the proliferative phase did not cause any obvious muscular reaction of the uterus. In 20 cases, when the emotional stimulus was applied in the secretory phase,

Table of Results. Summary of Data regarding Human Uterine Reaction to Emotional Stimuli.

Total No. of cases	Phase of cycle	Uterine motility before stimulus	Stimulus	Uterine motility after stimulus
17	Secretory	Contracting	Warned of imminent injection	Contraction increased
3	Secretory	Contracting	Possibility of injection mentioned	Contraction increased
10	Proliferative	Small contractions	Warned of imminent injection	No increase of contraction

the uterus immediately responded by a strong contraction. In 2 cases in this series the emotional stimulus consisted of applying cold packs to the skin of the lower abdomen. In 2 cases the patients examined were subject to moderately severe dysmenor-

rhoea. In both of these small groups the reaction in the secretory phase was a strong contraction of the uterus. In 4 cases the uterine reaction was looked for in the proliferative phase and in the secretory phase, and the reactions obtained corresponded to those already described.

Discussion.

Several pertinent questions arise regarding the emotional reaction of the uterus and its presence, apparently, only in the second phase of the menstrual cycle. What is the cause of the reaction in the secretory phase of the cycle? Why is there no response in the proliferative phase? Is it due to efferent stimuli from the higher centres? Is it due to an outpouring of adrenalin? Why, if it is due to adrenalin, does it not occur in the proliferative phase? Is the human uterus like that of the cat in its reactions to adrenalin, which, it will be remembered, shows different responses to adrenalin according to whether it is pregnant or not? In the pregnant cat, when presumably the uterus is under the influence of progesterone, adrenalin causes powerful uterine contractions. In the non-pregnant animal adrenalin causes inhibition and relaxation of the uterus.

None of these questions can be answered at present, but the problems they present are under investigation.

Summary.

(1). Using Moir's intra-uterine hydrostatic bag technique, the reactions of the human uterus to emotional stimuli have been noted in 30 cases.

(2). Emotional stimuli applied in 10 cases in the proliferative phase of the cycle produced no obvious response.

(3). Emotional stimuli applied in the secretory phase of the cycle produced uterine contraction.

My thanks are due to the Medical Research Council for a part-time personal grant for investigation on dysmenorrhoea, of which this study forms a part.

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[*A record of the discussion at the Congress of Obstetricians and Gynaecologists (Edinburgh, April,* 1939), *on Dr. E. Bandstrup's paper, "Some Problems Concerning the Aetiology and Treatment of Hyperemesis Gravidarum,"* (*p.* 710) *and that of Dr. E. M. Robertson's, "The Effects of Emotional Stress on the Contractions of the Human Uterus"* (*p.* 741), *appears on pp.* 759–61.]

A Case of Pregnancy in a Uterus containing Multiple Fibromyomata

BY

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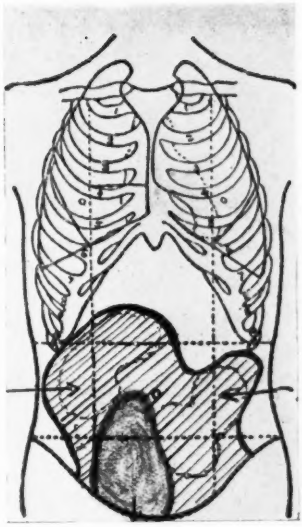
THE reason for publishing a case of pregnancy in a fibroid uterus, is that in this case it presents some unusual features and, therefore, seems worthy of record.

The patient, Miss X, aged 42, was admitted to the Presidency General Hospital, Calcutta on April 26th, 1938. She stated that she had a lump in the abdomen which she had been told by a doctor was a fibroid. Her last period had been from October 16th to 20th, 1937.

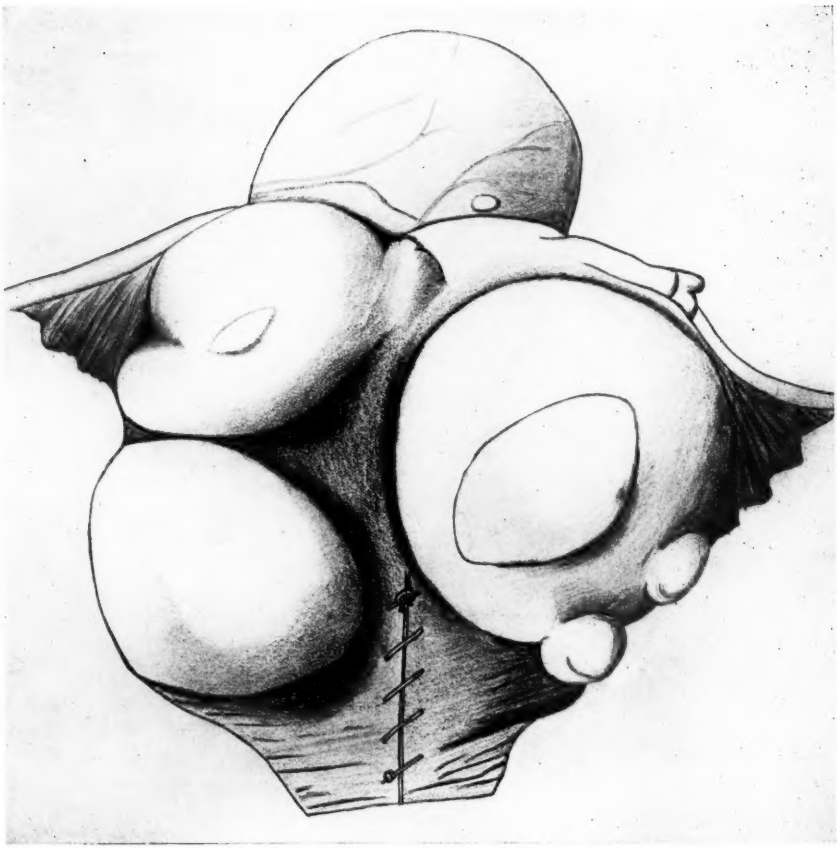
The patient was a great fat woman with pendulous breasts and abdomen. She first noticed the lump in 1934, and she stated that it had been slowly growing in size ever since then. Soon after she first noticed the tumour the periods had become profuse and painful. Since the previous October there has been amenorrhoea.

She was very fat, with huge pendulous breasts and abdomen, and was of the short stocky type with large, broad back and gluteal region. Her gait was of the waddling type. Her teeth, mouth, heart and lungs were normal. The breasts except for the excessive fat were normal. On inspection of the abdomen nothing but fat was apparent. On palpation, however, there was felt a large, lobulated mass. On the right side this tumour reached to the costal arch in the mid-clavicular line, but on the left side it stopped short of the costal arch by 2 inches. The general outline of the tumour was that of an Associaion football. In one part right in the mid-line, and low down, the tumour felt soft, but everywhere else it was hard and solid to the touch, and two distinct moveable tumours, the size of cricket balls, could be made out upon the main mass. (Fig. 1.)



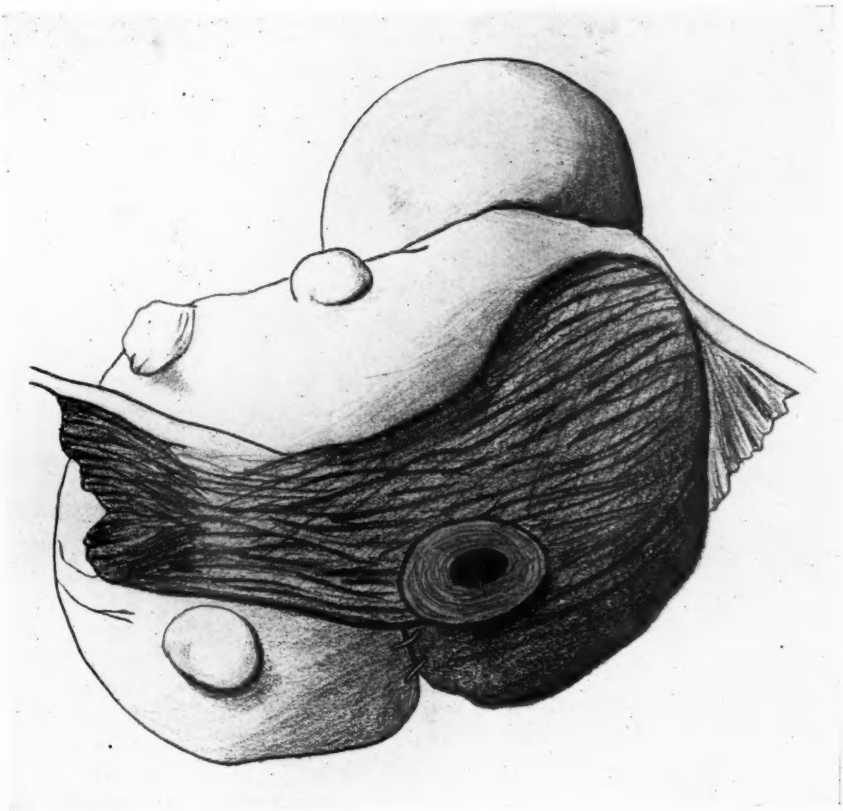
Soft area
(this was the pregnant uterus).

UTERINE TUMOUR (Weight 11 pounds).



FRONT VIEW SHOWING CAESAREAN INCISION AND FALLOPIAN TUBES.

UTERINE TUMOUR (Back view).



From abdominal examination the diagnosis was that the case was one of multiple fibromyomata in the uterus. The patient strained so much that vaginal examination without an anaesthetic was impossible. She was anaesthetized and a vaginal examination carried out. This confirmed the abdominal diagnosis, but in addition revealed the fact that the soft part of the tumour which was felt in front, was a pregnant uterus. The foetal skull could easily be felt in the lower pole of the uterus, and other parts of the foetus could be made out higher up. The cervix was very soft and could be dilated easily with the examining finger. It was flabby and seemed liable to tear.

On the next day, when the patient was told what was the matter with her, she indignantly denied the possibility of a pregnancy, and in spite of assurance that a mistake in diagnosis had not been made, she persisted that it was impossible, so a skiagram was taken which showed the skeleton of a foetus of about $5\frac{1}{2}$ months. She then changed her attitude and admitted that she had been married 2 years previously but, to use her own words, her husband was such a "drunken out-of-work rotter" she had turned him out of her house almost immediately after the wedding, and that sexual intercourse had not taken place. She then went back to her own work which was that of private nursing.

The patient did not see her husband again until early in November 1937, when one night he came to her flat and said that he was going off the next day to a job, and that as he had nowhere to sleep he had come to ask her to take him in for the night. This she did, and then he demanded his rights as a husband, and as he threatened violence if refused, she accepted. She informed me that this was the only time in her life that she had had sexual intercourse, and I have no reason to doubt her. She was somewhat anaemic, her red-blood count being 2,700,000. She was, however, in a good state of health otherwise, her urine being quite normal, and her cardiac apparatus being excellent, It was considered extremely unlikely that any attempt at induction would be successful and, indeed, any such procedure was contra-indicated owing to the fibroid condition, especially of the lower pole of the uterus,[1] and as an operation would have to be done at some time in order to remove the tumour, I decided to operate. The patient was, therefore, treated with campolon, iron and calcium, and when the red-blood count had reached 3,500,000 per c.m. I operated; this was on May 10th.

The abdomen was opened by a right-sided paramedian in-

incision extending from 2 inches below the ensiform cartilage to the symphysis pubis. An endeavour was made to deliver the whole mass through the abdominal wound as I wished to remove the uterus complete with all its tumours, and the foetus *in utero*. This was found to be impossible owing to the difficulty of retracting the fat sides of the abdomen far enough, and also because the upper right-hand pedunculated tumour was stuck fast under the costal arch. The uterus was determined, and hysterectomy performed. The foetus was delivered and the uterine wound closed. The rest of the tumour, that is, the uterus with all its fibromyomata, was removed by subtotal hysterectomy; the appendix was removed, and the wound closed in the usual way. Convalescence was uneventful, and the patient left hospital quite well on June 9th.

Discussion.

Pregnancy in a fibroid uterus is by no means an uncommon occurrence. Indeed eminent authority states that only 30 per cent of women with fibroids are sterile.[2] There are, however, some types of fibroids which are more prone to give rise to sterility than others. The pedicled, subserous fibroid is not likely to be a cause of sterility, but if situated in the lower pole of the uterus it may be a serious bar to a successful conclusion of labour. Situated in other parts of the uterus it may not cause any trouble at all during labour, and even when in the lower pole it may rise up out of the pelvis and not interfere with the labour. Multiple tumours of this type cause more trouble than single ones.

As to how far fibroids of the other types, that is intramural and submucous fibroids, are in themselves the cause of sterility, is a matter for conjecture. De Lee[3] states that women with such tumours are frequently sterile.

Providing the Fallopian tubes are not occluded by the presence of the tumour in the neighbourhood of the cornua of the uterus, and that a secondary change has not taken place in the tumour which by giving rise to salpingitis causes sterility, there does not appear to be any evidence to convict the fibroid *per se*. Fibroids of this nature, especially in the lower pole are, however, nearly always a cause of dystocia, which is a different matter. The case under consideration had several subserous and several intramural fibromyomata, and yet became pregnant. The patient was well known in the hospital as she is a nurse doing private nursing in Calcutta. She is a quiet, respectable woman,

and as her marriage was kept a secret she was known to them all as "Miss X". Consequently, until the full facts were known, the diagnosis of her condition caused astonishment. The chief points of interest in the case are as follows:—

1. Pregnancy is less likely to occur in a grossly obese woman, than in one of normal weight.

2. Pregnancy is less likely to take place after the woman is over the age of 40 years.

3. Pregnancy is less likely to take place in a fibroid uterus than in a normal one.

4. A drunken, debauched, elderly man is less likely to be a father than a young, virile one.

The patient was obese, elderly, her uterus was crowded with tumours, her husband was elderly, and unfit, and yet she became pregnant after one act of coitus. Except for the amenorrhoea there were none of the usual signs and symptoms associated with pregnancy. There was no morning sickness, no pigmentation of the face, and though the foetus was alive, no quickening, and no change in the breasts. The latter were already so large that further enlargement, if any, passed unnoticed, while the amount of fat on the abdomen, plus the tumour which has been growing in size for months, cloaked the presence of the foetus. Indeed if the pregnancy had not been so advanced when the patient came to hospital, when the case was unmistakable, and had been say one of 3 months, it might only have been discovered at operation. The amenorrhoea was the only symptom of pregnancy. The special points noted in this case are, I think, of sufficient interest to warrant publication.

Description of the Tumour.

The tumour is one of multiple fibromyomata of the uterus. The whole is a heterogenous mass weighing 11 pounds. Hysterectomy has been performed and the wound sewn up.

On the front of the uterus are four large subserous fibromyomata, each about the size of a cricket ball. One of these has three smaller fibromyomata superimposed upon it. Two others have one small fibromyomata each, and the last is free.

The postero-inferior view shows three smaller subserous myomata, and in this view the general fibromyomatous condition of the intramural type can be seen. In order to preserve the appearance of the specimen it was not split up.

My thanks are due to Sister Leonard, my theatre Sister, for the drawings of the specimen.

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Radium Treatment of Menopausal Haemorrhage, followed by Carcinoma of the Body of the Uterus Three Years later

BY

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THE treatment of benign bleeding associated with the menopause by an intra-uterine application of radium is recognized as an eminently satisfactory procedure. It is an example of conservative gynaecology, by which many women have been spared a radical operation for removal of the uterus. Provided there is no organic disease or tumour in the uterus or endometrium, cure is effected in a very large proportion of cases. It has not been decided whether the action of the radium is on the uterus or ovaries, or both, the latter is probably correct. There is certainly some action on the uterus.

The question arises whether carcinoma of the body of the uterus ever follows this treatment, and, if so, whether it is in any way a remote effect of the application of the radium. Until recently I had not seen a case and had formed the opinion that there was no risk of such a sequela. This opinion has now been challenged by a case of which the history is as follows:

The patient, a widow aged 51 years, who had had one child 20 years previously, was seen by me first 3 years ago, suffering from uterine haemorrhage. Her history was that the periods had been regular until about 18 months previously. Then the periods began getting less frequent, and during the previous winter she had had amenorrhoea for 6 months. In April, 1935, she went to America, and had amenorrhoea until August. The next period occurred in October, about the time of her arrival in England on October 6th. This period did not stop, and she saw something every day until 5 weeks later, when she had another period. There was not any pain or any other symptoms. On examination the

cervix appeared normal and the uterus slightly enlarged. Exploratory curettage was performed on November 18th. The uterine sound passed $3\frac{1}{2}$ inches. Dilatation and curettage were performed and, as there were no signs of tumour or disease, 50 milligrams of radium element were inserted into the uterine cavity for 36 hours. The radium consisted of two 25-milligram tubes, made of platinum, 1 milligram thick, placed end to end in a silver applicator, surrounded by rubber tubing. The microscopic report on the endometrium by Dr. Ingram stated: "Sections show highly convoluted mucous glands in an active state of secretion corresponding to the immediate premenstrual condition. I find no evidence of new growth."

The patient was cured of her bleeding and remained well until exactly 3 years later, November 18th, 1938; she then had a little bleeding and blood-stained discharge for a few hours. This stopped for 24 hours and then recurred. On examination the uterus was felt to be definitely enlarged, and immediate hysterectomy was advised. This was carried out 3 days later, when the whole uterus was removed with the ovaries. On examination after removal the uterus was seen to be enlarged; it measured 4 inches long by 3 inches wide at its widest part. The surface of the uterus appeared quite smooth. On bisecting the uterus, the uterine wall was thickened and the cavity was enlarged. The lining of the uterus was irregular and its colour was patchy. In certain areas there was invasion of the uterine wall by the deeper parts of the endometrium. The macroscopic picture was that of adeno-carcinoma, and this was confirmed by the microscope report by Dr. McNaughton, which was as follows:

> "Wide and deep invasion of uterine wall by an irregular growth of columnar-celled carcinoma. In the deeper parts, glandular structure is, for the most part, almost entirely lost, and the growth is here represented by irregular columns and groups of undifferentiated polyhedral cells, separated from each other by a scanty stroma. Considerable areas of degeneration are present with invasion of polymorphonuclear cells, indicating a slight pyogenic infection."

This is the only case in my own experience in which carcinoma corporis has occurred after previous radium treatment. In looking through the literature, however, the following references to this subject have been found:

In a series of 200 cases treated in Liverpool, Malpas[1] reports one case of subsequent corporeal carcinoma. This occurred in a 2-para aged 49 who had an intra-uterine application of radium

Bisected uterus after removal showing carcinoma corporis.

of 40 milligrams radium element for 40 hours, equalling 1,960 mg. hours, for benign bleeding. The uterus was 3 inches long, and microscopic examination of the curettings did not reveal any malignant changes. Amenorrhoea followed for 20 months, then symptoms of discharge and pain occurred, and hysterectomy was performed. The uterine wall was infiltrated by a columnar-celled carcinoma.

Martindale[2] reports one case in which carcinoma was found one year after radium treatment. Bland[3] records one case in which carcinoma was found 3 years after radium treatment. Schintz[4] reports two cases occurring 1 and 3 years respectively after radium treatment for fibroids. Naujoks[5] reports one case of his own occurring 3 years after radium treatment, and quotes three other cases. Leda Stacey[6] records two cases, one occurring after a dose of 600 mg. hours and one which was found $2\frac{1}{2}$ years after radium treatment of 500 mg. hours for fibroids.

Essen Moller[7] states he had six cases of corporeal carcinoma after radium castration, and has accordingly abandoned the method. He considers the carcinoma may have been consequential upon the treatment and that this danger is very real.

The points which arise for discussion are whether, in the reported cases, the carcinoma was already present at the time of radium treatment or whether it was a result of the treatment. The rarity of this occurrence seems to make it improbable that the new growth was the result of the previous radium treatment. It seems more likely that carcinoma would have occurred in any case or that carcinoma was present when the curetting was performed and that the curetting and microscopic examination failed to detect the new growth.

In my own case, the length of time, 3 years, which elapsed between the radium treatment and the subsequent carcinoma makes me incline to the opinion that the onset of carcinoma was in no way consequential upon the previous treatment with radium.

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Two Unusual Cases of Ectopic Pregnancy

BY

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CASE I.

UNILATERAL twin ectopic pregnancy is a comparatively rare condition. Falk and Blinick,[1] having reviewed the literature and described 2 cases of their own, state that 65 is the number of authentic cases reported. The purpose of this communication is to increase that total by one.

A woman, aged 26 years, pregnant for the first time, was admitted to the Glasgow Royal Maternity and Women's Hospital on August 9th, 1938, with the following history. Her last menstrual period occurred on May 7th, 1938, making the duration of pregnancy approximately 13 weeks. For the first month of pregnancy the patient was perfectly well, but she then began to experience a dull pain, low down on the right side of the abdomen. On July 12th, when she was about 9 weeks pregnant, she was admitted to a general hospital as a case of appendicitis, but, after observation for four days, was discharged. Since leaving that hospital she had had occasional vaginal bleeding, and the dull, right-sided abdominal pain had returned.

On admission to the Glasgow Royal Maternity and Women's Hospital, the patient looked well nourished, although rather pale. A tender swelling was palpable in the right iliac fossa. The following morning, bimanual examination was carried out, and the diagnosis of right-sided tubal pregnancy, unruptured, was made. Incidently, a complete decidual cast came away on the examining fingers.

Under spinal anaesthesia the abdominal cavity was opened, and the diagnosis confirmed. Right salpingectomy was performed. The ovaries and left Fallopian tube were normal. The unruptured sac measured $3\frac{1}{2}$ inches by $2\frac{1}{4}$ inches. When opened,

FIG. 1.

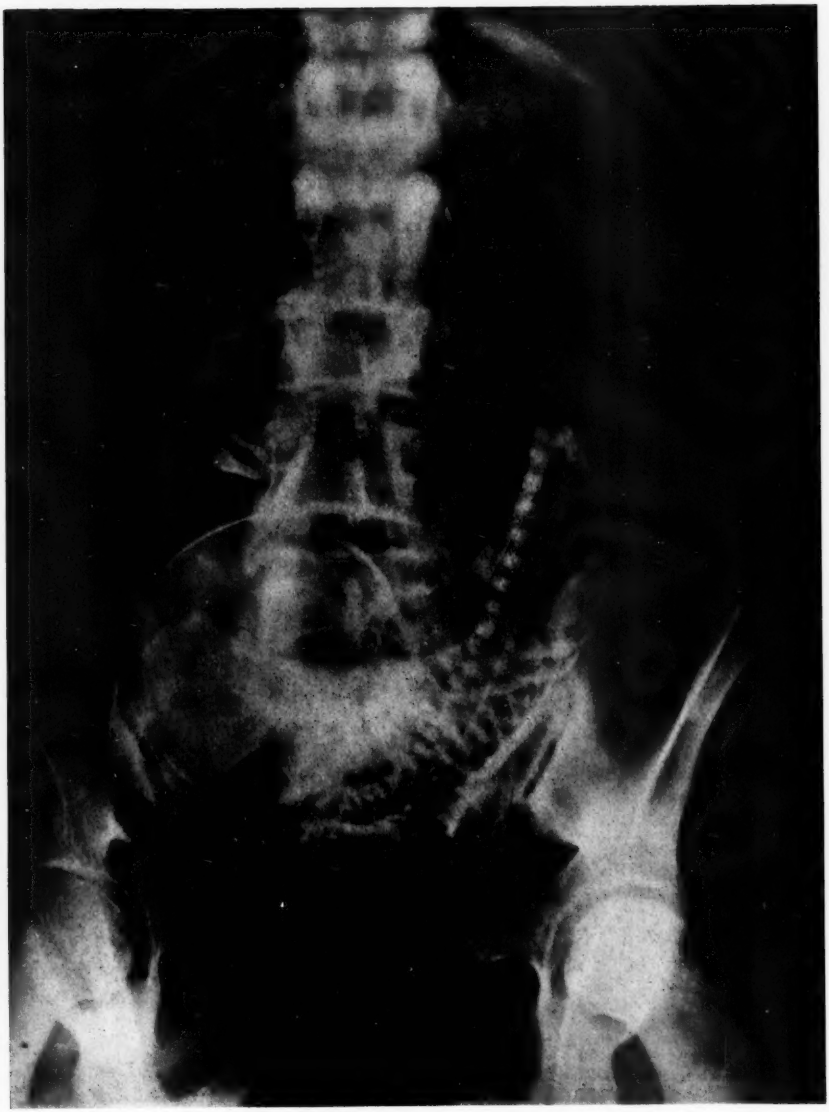

FIG. 2.

FIG. 3.

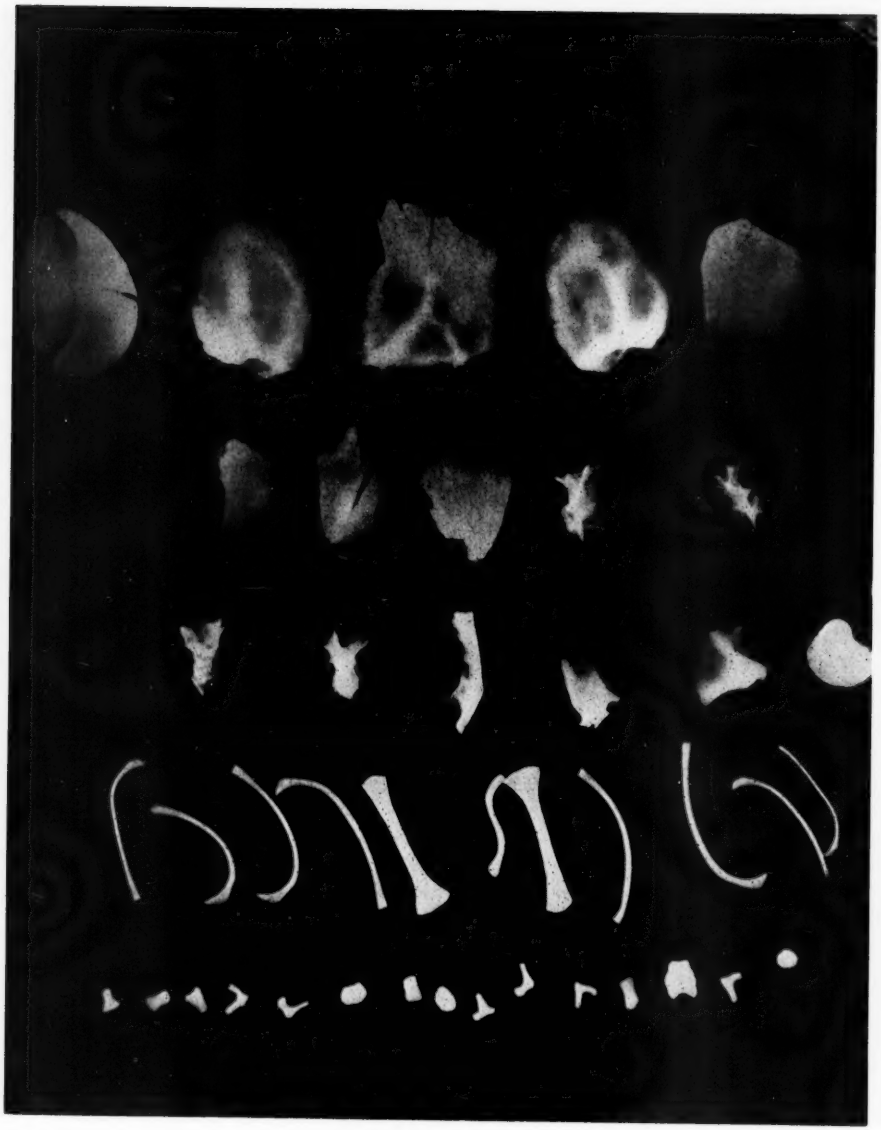

FIG. 4.

crystal-clear liquor amnii escaped, and the condition was seen to be an example of uniovular twin pregnancy.

The photograph shown (Fig. 1) was taken after the specimen had been in formalin for three months. Convalescence was uneventful, and the patient left the hospital 15 days after operation.

Case II.

Before operative intervention became the routine practice in cases of ectopic pregnancy, the products of conception frequently found an exit by the bowel, bladder, or abdominal wall. The following notes record the essential features of a patient who has been delivered of foetal remnants *per rectum* at intervals over a period of several months. The final foetal instalment was removed on November 8th, 1938, exactly 18 months after conception.

A woman, aged 32 years, was admitted to the Glasgow Royal Maternity and Women's Hospital, on January 7th, 1938. She had suffered from diphtheria at the age of 10 years. There were 4 previous pregnancies, all proceeding to term, and all resulting in spontaneous deliveries except the first, which was instrumental. The puerperium in all instances was uneventful. All the children are alive except the last.

The last menstrual period began on May 2nd, 1937, making the expected date of delivery February 9th, 1938, and the maturity at the time of admission 36 weeks.

Since the third month of pregnancy the patient was troubled with shooting pains intermittently in the lower abdomen. At no time did she feel life, and she thought that her abdomen was not increasing as she might expect. On two or three occasions, she passed matter by the bowel, and thought she had a bowel abscess.

At 11-30 p.m. on the night prior to admission, a fairly brisk vaginal haemorrhage occurred; this recurred, and at 4 a.m. on the day of admission she passed, *per vaginam*, a small mass of tissue, after which there was little or no bleeding.

The patient appeared pale. The abdominal swelling suggested pregnancy of 24 weeks' duration. Foetal parts were not palpable, and the foetal heart was not audible. The cervix was tightly closed; the uterine body was hard and only slightly enlarged. Sections of tissue passed *per vaginam* were reported by the pathologist as "necrotic decidua showing in places small

fibrillar masses which suggested colloidal material, these masses lying free in the decidua like foreign bodies".

Following pyrexia (as high as 103.2°F) of 2 weeks' duration, loose, offensive faecal matter, mixed with blood, was passed on February 18th, 1938, and the temperature became normal. The patient looked pale and ill. Painless diarrhoea continued, the colour of the motion being frequently dark grey. On June 27th, 1938, the the patient developed backache and was sick; she appeared dehydrated and toxic. In the foul-smelling faecal matter, numerous foetal bones were observed for the first time. On two occasions thereafter, foetal bones were passed *per rectum*. During the period between August 8th and November 8th, 1938, the patient was anaesthetized on four occasions, when bones, mostly cranial, were removed digitally *per rectum*. The patient left hospital on November 21st, 1938, having spent there, in all, 211 days; this protracted residence was, however, punctuated by several holidays at a convalescent home.

Of the numerous X-ray plates taken only 3 are reproduced, Fig. 2 was the first taken, Fig. 3 at a considerably later date, while the last, Fig. 4, portrays the foetal bones delivered *per rectum*, spontaneously and digitally.

The policy of non-intervention is abundantly justified in this case. When seen 3 months after leaving the hospital, the patient had menstruated once normally, and her weight had increased from 4 stones 10 pounds, to 7 stones 10 pounds, and the bowels moved regularly.

I am indebted to Professor James Hendry, to whose wards both patients were admitted, for permission to record these notes.

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Congress of Obstetricians and Gynaecologists in Edinburgh, 1939

DISCUSSION ON THE PAPER OF DR. E. BANDSTRUP ON "HYPEREMESIS."

(*See pp.* 700–710.)

PROFESSOR HENDRY congratulated our welcome visitor from Denmark on the important paper which he had just read. Dr. Bandstrup's perfect English was appreciated very highly by his insular audience, and deserved a very special congratulation.

Dr. Bandstrup had demonstrated in his paper that still one more specific aetiological factor in hyperemesis had been discredited. In the Research Department of Glasgow Royal Maternity and Women's Hospital, Dr. Sheehan, whom he hoped would take part in the discussion, had failed to find any constant abnormality in the suprarenal glands in fatal cases of hyperemesis.

Professor Hendry desired an opportunity of communicating to the Congress the results of what might be described as the non-specific treatment of hyperemesis gravidarum. This treatment is based on general metabolic considerations, and not on a specific aetiological factor. There are three, or possibly four, factors which require to be considered in treatment. In the first place, the patient suffering from hyperemesis gravidarum requires the administration of large amounts of fluid to counteract the dehydration. The patient requires a large amount of glucose to replenish the diminished store of carbohydrate in her liver and her tissues. The psychic factor in the condition should be dealt with by the administration of sedatives. There may be some relation between the carbohydrate disturbance, the sympathetic nervous system, and the psychic factor in those cases. We are not quite certain at the moment how far we must regard this condition as also associated with avitaminosis, particularly with regard to vitamin B.

It is of the greatest importance in the treatment of cases of hyperemesis that the medical and nursing staffs carrying out treatment should form a good team and be absolutely confident of success. Professor Hendry's own staff had gained very great experience in this work and he would prefer to have any one of his private patients admitted to his wards at Glasgow Royal Maternity Hospital for treatment rather than to the best staffed and best equipped nursing home in the city. The staffs of such homes should only be regarded as amateurs in the care of a case of this kind.

Professor Hendry might have been happier in making his communication 18 months ago. At that time, over a period of 3½ years 85 cases of hyperemesis gravidarum had been treated in his wards at Glasgow Royal Maternity

and Women's Hospital with only one fatal case, and only one in which it was found necessary to terminate the pregnancy. He would then have made the mistake, of course, of reporting on too small a series. The series now extended to 5 years and included 110 cases which had been classified on a broad clinical basis as follows: mild cases, 64; moderate cases, 27; severe cases, 19. This gave over 40 per cent. of moderate and severe cases. The essential method of treatment in this group was the administration of intravenous glucose, either by large amounts given at one time, or by the continuous drip method, the latter being preferable. The sedative effect was secured by the administration of rectal salines containing usually bromides, but sometimes luminal. Recently, in one or two cases concentrated preparations of vitamin B had been given intramuscularly. Of the series of 110, 106 were dismissed in satisfactory condition, one of them after a spontaneous abortion. There were 4 fatal cases, i.e. a mortality of 3.63 per cent. Three cases, including two of the fatal cases, had the pregnancy terminated by an abdominal hysterotomy, i.e. an incidence of interference of 2.73 per cent. It is interesting that of the 105 cases in which the pregnancy was conserved, 4 cases developed toxaemia in the later months, including one case of postpartum eclampsia, but all made satisfactory recoveries. Five of the patients were re-admitted to the wards later on account of the recurrence of hyperemesis. Of those, one had the pregnancy terminated by abdominal hysterotomy and did well; another had a spontaneous abortion and did well; a third developed parotitis, and is referred to later among the fatal cases; the remaining 2 were severe cases but did well on conservative treatment.

Of the 4 fatal cases, the first was originally admitted as a mild case and dismissed well; 11 days later the patient was re-admitted as a severe case; she responded fairly well to treatment, but developed acute parotitis; she was transferred to general surgical wards and died from septicaemia 12 days later. The second was a severe case of long duration; the patient had been treated for many weeks in a cottage hospital, and was admitted to Glasgow Maternity Hospital *in extremis*. She made little response to treatment and died 4 days after admission; the liver showed fatty changes only. The third was a severe case; there had been one previous pregnancy terminated for hyperemesis. This patient improved during treatment with intravenous glucose by the drip method, but relapsed into coma; she improved slightly when abdominal hysterectomy was carried out; the benefit was only temporary. At the post-mortem examination fatty changes were found in the liver, and there was a terminal bronchopneumonia. The fourth was also a severe case; the patient had been ill for 5 weeks before admission; she was given continuous intravenous glucose by the drip method for 10 hours with improvement; she had visual disturbance amounting to blindness, and was drowsy. Abdominal hysterotomy was carried out with temporary improvement but she relapsed soon afterwards into coma and died 32 hours after admission. Post-mortem examination showed fatty changes in the liver, but in this case permission had been secured to examine the brain and Wernicke's encephalopathy was found. Dr. Sheehan will give further information about the post-mortem findings in such cases.

In designing treatment for patients with hyperemesis gravidarum we can at present regard them only as cases of progressive starvation with a marked psychic factor. The earlier the stage at which such patients are admitted to hospital, the better the prognosis.

DR. LENNIE drew attention to the appalling type of hyperemesis which was prevalent in Glasgow. He referred to the high figures quoted by Professor Hendry which represented only one unit, and to the fact that there were three such units in the Royal Maternity Hospital. It was his personal opinion that hyperemesis was the most treacherous complication in pregnancy. The borderline between the so-called neurotic vomiting and the much more serious or toxic variety might be very narrow. Some controversy had been raised with regard to the question of a neurotic or psychological cause as being responsible for the vomiting. He did not think that it had been sufficiently stressed that the temperament of those women underwent a definite change as a result of the disease. A normally charming and vivacious woman would become irritable, morose and difficult. This change in temperament was apt to engender antagonism on the part of the doctor or nurse, who concluded that the woman was scheming to get rid of her pregnancy. In the case of the unmarried woman this seemed even more obvious. He had known of several cases in which a life had been lost on account of this antagonism.

Various grave symptoms had been mentioned, but he would like specially to stress the importance and gravity of nystagmus. He had first observed this phenomenon in 1924 in a woman who was desperately ill, and who died despite immediate evacuation of the uterus. He was so impressed by its importance as a grave prognostic sign that during the succeeding years special observations were made and its importance confirmed. In his unit all assistants and house-surgeons now look for nystagmus as routine in cases of hyperemesis, and when elicited the pregnancy is terminated forthwith. A delay of 24 hours may prove fatal.

Some speakers had expressed doubt as to a brain lesion ever being present in hyperemesis. He would like to refer to a specimen in the possession of Dr. Sheehan, of the Research Department of the Royal Maternity Hospital, in which multiple small haemorrhages can be seen in the corpora mamillaria and walls of the third ventricle. This patient died of toxic hyperemesis. The specimen explains the cause of nystagmus and solves a problem which for long has been obscure. Cerebral lesions undoubtedly do occur in the most serious cases.

Dr. Lennie did not agree with Professor Browne that abdominal hysterotomy was the only method which should be used to terminate a pregnancy in cases of hyperemesis. He contended that evacuation of the uterus *per vaginam* by means of Hegar's dilators and the finger was in the majority of cases the method of choice.

DR. BANDSTRUP, replying, said:

I wish to thank you for the kind reception you have given my paper and for the interest shown by those who have taken part in the discussion.

To Professor Hendry I should like to say that the non-specific therapy adopted by Professor Hendry runs along the same lines as followed in the Lying-in Department A of the Rigshospital, Copenhagen. I fully agree with Professor Hendry that the psychological treatment is extremely important, and that it is of particular importance that the nurses are used to take care of this special kind of patients.

Dr. Sheehan's remarks on the pathologic-anatomical findings in hyperemesis are of the greatest interest since the literature on this subject is scarce, and I have no personal experiences in this respect, as my 40 fatal cases were not submitted to systematic autopsy. I am especially interested to hear that Dr. Sheehan has found no abnormalities in the suprarenal cortex in fatal cases of hyperemesis, as the scanty reports of alleged atrophy of this organ in hyperemesis require confirmation or refutation. I think that Dr. Sheehan's findings ought to be published in detail.

Professor Strachan's distinction of toxic and neurotic cases seems right to me, in so far as there certainly are cases in which the neurotic factor is predominant, while other cases from the very onset appear to be severe and non-neurotic. In many cases, however, the two factors are mixed up, and you may see an initially neurotic case gradually get very malignant, or more suddenly. Even when the patient is a hysteric or a simulant, the case may become malignant. Once I have seen a case in which the patient entered the hospital and wanted to get rid of the foetus; she put her finger in her throat to produce the vomitings, and yet, finally, she was so ill that she came near dying. In lectures on this subject I used to tell the students that the peculiar thing about emesis is that, to begin with, the patient may be hysterical, and later she may be—dead. Hence the doctor has to watch her condition very carefully.

I think, therefore, that a sharp distinction between toxic and neurotic cases would not be useful clinically.

To Professor F. J. Browne: I thank you for the very kind interest you have taken in my paper. As to your impression of the disease being more severe in some parts of the country than in others, I am able to affirm that statement—without being able to give any figures as evidence. I think that in Denmark most of the severe cases are met with in the country.

Professor Browne emphasizes that our results regarding the figures for excretion of gonadotropic hormone during pregnancy are in conflict with those obtained by other investigators, including his own. I think the technique employed by us for estimation of gonadotropic hormone—described by Hamburger and by Bjergaard—is reliable. Details regarding the technique and the value obtained with it will be published later in *Acta Obstet et Gynec. Scandinav.* The values obtained by us have not been higher than may be found in normal pregnant women, in whom the figures may be very high, occasionally even in the third or fourth month. And we have not been able to find any proportionality between the figures for the output of gonadotropic hormone and the clinical condition of the patient. But I shall willingly admit that the number of our patients examined in this respect is few, and, with exception of one, the cases were not of the more severe type. Further

investigation of this question is needed, and the same applies to the output of pregnandiol.

Professor Browne suggested that the gonadotropic hormone excreted might be of pituitary origin. In some cases in which the urine showed a high titre for gonadotropic hormone, we also injected the urine into infantile cockrels, in order to see whether the hormone was of hypophyseal or chorionic origin. The cockrels showed no change in the testes or comb that would indicate the presence of gonadotropic hormone of hypophyseal origin. So we were able to demonstrate only the presence of chorionic gonadotropic hormone in the urine.

I have no experience in Professor Browne's technique for interruption of pregnancy in the abdominal way, but to me it seems rather tempting. As a matter of fact, in many cases of hyperemesis the pregnancy will have gone on to the fourth month or longer, and at that time you cannot be sure of avoiding violent haemorrhage in inducing abortion *per vaginam*.

Professor Murray touched on the interesting question of the late hyperemesis, that is, hyperemesis in the last third of pregnancy. I am not sure that it exists in the sense of a disease with the same clinical features as are seen early in pregnancy. In our material, therefore, I have excluded the late hyperemesis cases. Most often the vomiting late in pregnancy is associated with pre-eclamptic toxaemia or with pyelitis; or it may be of purely mechanical origin, the stomach being pushed up and compressed by the large uterus.

Finally, I wish to emphasize that some of the fatal cases in my material are collected from small hospitals where cases of hyperemesis may be so rare that the doctor has forgotten that women may die of this disease. But our patients ought *not* to die of hyperemesis, as we have it in our hand to cure the patient by timely interruption of the pregnancy. And we must not forget that if in some cases we terminate pregnancy too early, we only lose the foetus, and the patient may have a child another time. But if we interrupt pregnancy too late, we lose both the child and the mother—and there is no possibility of a later pregnancy.

DISCUSSION ON THE PAPER OF DR. E. M. ROBERTSON, ON "UTERINE MUSCLE ACTIVITY."

(*See pp.* 741–747.)

Dr. J. K. Sutherland showed five slides illustrating tracings of uterine contractions obtained using the same technique. The first three were examples of the effect of the injection of pituitrin in the secretory phase of the cycle. A positive reaction was observed in each case. Examination of the slides would indicate whether the stimulation caused by the injection had augmented contractions. On one this appeared to be true, in the second probable, but in the third there was no reaction. The other two slides illustrated the alleged

oxytocic effect of benzedrine sulphate. (Boyd, *Amer. Journ. Med. Sci.*, April, 1938). The tracings were taken from puerperal uteri and it would appear that the drug has a mild stimulating action on the puerperal uterus. This effect had been obtained in about 6 out of 12 cases tested, the drug being given by mouth.

Dr. Sutherland referred to cases of primary dysmenorrhoea in which an oestrin (stilboestrol) withdrawal bleeding had occurred and was entirely painless, whereas the period both before and after this bleeding was accompanied by the usual pain.

THE SEVENTEENTH NATIONAL CONGRESS OF OBSTETRICS AND GYNAECOLOGY

The Seventeenth National Congress of Obstetrics and Gynaecology is to be held at Turin on October, 15th, 16th, 17th, 18th, 1939. The President of the Governing Committee is Prof. E. Cova.

The scientific agenda is as follows:

First paper: "The gynaecological symptoms of extra-genital morbid processes" (Prof. Vozza).

Second Paper: "Hormonic therapy of the ovaries in obstetrics and gynaecology" (Prof. Maurizio).

The following subjects will then be discussed:

(*a*) Obstetric and gynaecological radiology (Prof. Bortini, Prof. Quinto, Prof. Robecchi).

(*b*) Painless delivery (Prof. Dallera).

(*c*) The gynaecological damages of birth control practices (Prof. Clivio).

Members may submit two papers, preferably on an analogous subject, and may send in their names now.

It should be borne in mind that the prize "Guzzoni degli Ancarani" of Lit. 2.500 reserved to members of the Italian Society of Obstetricians and Gynaecologists who are not professors or lecturers, will be allocated in preference in 1939 to works on analogous subjects.

Members of regional societies are eligible for admission to the Congress, as well as any medical man. The entrance fee is fixed at L.60 and at L.30 for assistants. This is payable to the Comitato Orindatore del Congresso, Regia Clinica Ostetrica, Ginecologica, Via Ventimiglia, Torino.

Doctors attending the meetings may take part in the discussions and submit papers.

The titles of the papers should be forwarded as soon as possible, in any case on or before the 15th September next, to the Committee.

Those wishing to become members before the Congress should

apply to the President of the Society, Regia Clinica Ostetrica e Ginecologica, Turin, stating his qualifications and the subjects in which he specializes.

To all national and regional members, as well as to those intending to be present, who will forward their entrance fees in time, the Committee of the Congress will send the final programme before the 10th October, permit entitling holders to reduction on railways, list of hotels, etc.

BOOK REVIEWS

"Endocrinology in Modern Practice," by WILLIAM WOLF, M.D., M.S., Ph.D., Endocrinologist to the French Hospital; Attending Endocrinologist, Misericordia Hospital, New York. Second edition; 1,077 pages; 176 illustrations. Price 45*s*. W. B. Saunders Company, Ltd., London and Philadelphia.

THE production of any book involves a great deal of trouble, and when faced with a work of this type, containing over a thousand pages and 176 illustrations, at a price of 45*s*., one hesitates to pronounce a complete condemnation. The reviewer has studied this volume carefully, and regrets that it is impossible to follow any other course. The author has attempted to give a complete account of the theory and practice of endocrinology. It is doubtful whether one person is competent to undertake such a task; a review of the physiological and biochemical aspects of any single hormone is a considerable achievement, and to attempt to cover all the hormones from every aspect would appear bound to fail.

It is not clear from what angle the author has tried to regard the subject. The book opens with a peculiar dedication, which runs as follows:

"This book is dedicated to the unsung hero of the healing art who is ever ready to expose himself at the front in the struggle against infirmity and disease. His weapons are compassion, knowledge and skill, combined into a glorious power which vanquishes the forces that obstruct the road to health and happiness." Any attempt at a detailed criticism would simply irritate the reader and the author, and will not be given here. It is enough to say that nearly every conceivable error is made. The same illustrations occur twice, and there are serious omissions; for example, corticosterone and desoxy-corticosterone are not mentioned, although the book was published in 1939. There is not a single reference, so that the reader has to rely entirely on the author, which is unfortunate. There are a series of novel features, which in the reviewer's opinion add to the disadvantages of the book; for example, elaborate but valueless summaries, which have the appearance of a railway time-table, are given at the end of every chapter.

The book's usefulness as regards endocrinology in practice may be illustrated by a typical quotation from the chapter on "Diagnostic Procedures in Endocrinopathic Conditions," page 933, describing a test recommended by the author:

"The Schellong test, in which blood-pressure readings are made before and after exercise, shows that in one-third of pituitary disorders the blood-pressure declines after exercise, in another third remains unchanged, and in the third group shows a rise."

In the chapter on "Symptom Diagnosis" there is a list of symptoms and the conditions in which they occur which includes such items as large head, small head, large round face, expressionless face, adenoidal expression, and receding chin.

The book is characterized by long-windedness and a complete lack of essential detail when dealing with modern procedure; for example, aspects of the Friedman test occupy half a page, and if these directions alone were followed there might be serious consequences. In the chapter entitled "Commercially Available Endocrine Products," the author has spent much time in compiling a list of most of the endocrine products on the market, good, bad, and indifferent, and he repeats the commercial claims of each one. He says that "limitations in space, personal experience, and the advice of confrères . . . in a large measure helped in the decision of what to include and what to omit." One can only assume that he is unfortunate in his friends, as by far the larger part of the substances he mentions are quite inactive; for example, he includes thymus preparations, extract of mammary glands, and whole desiccated adrenals by mouth. In the discussion on the use of the preparations further indiscretions are committed, and the author, with fatal accuracy, has reproduced practically all the exploded myths of endocrine therapy; thus the adrenal cortical hormone is recommended for low blood-pressure, allergic states, tuberculosis, dementia praecox, Paget's disease, carcinoma, and cyclic vomiting and infantile diarrhoeas.

"Menstrual Disorders: Pathology, Diagnosis and Treatment" by C. FREDERIC FLUHMANN, B.A., M.D., C.M., Associate Professor of Obstetrics and Gynaecology, Stanford University, School of Medicine, San Francisco, California; Fellow of the American Gynaecology Society. Philadelphia and London: W. B. Saunders Company, 1939. (Pp. 329; 22*s*. 6*d*.)

THIS volume on menstrual diseases by Professor Fluhmann is a very valuable addition to the general literature on this important subject, and is one of the first modern and up-to-date accounts of menstruation and menstrual disorders in the English language. The author is well-known as a pioneer worker in the field, and it is, therefore, with considerable pleasure that we welcome his book. In the three hundred odd pages will be found an excellent account of the very complex series of changes occurring in the normal menstrual cycle and the variations which are associated with the different pathological conditions affecting the cycle. Professor Fluhmann gives a historical account of the study of the subject, and then proceeds through a discussion of puberty and the establishment of the menstrual cycle to the various morphological changes which take place. The microphotographs illustrating these sections are of a very high order of excellence, and do much to make this very difficult subject clear. There are two chapters on the sex hormones, one dealing with the hormones themselves, and the other with the endocrine control of menstruation. The chapter on the sex hormones is not quite so full as some would

have wished, but, as the author points out, he is writing primarily for clinicians. It is perhaps a pity that the chemical work on the hormones is not given in greater detail, since most clinicians are not aware of the vast strides that have been made in this branch. Professor Fluhmann's information, however, is accurate and quite adequate from a general point of view. The chapter on modern methods of investigation is too full for the general reader, and not full enough for the person who actually wishes to perform the tests, while a number of the tests described are not regarded in this country as being of any value; for example, the estimation of blood-oestrogen and the estimation of oestrogen in the urine of non-pregnant women is not believed to be of any assistance to diagnosis. The various menstrual disorders such as amenorrhoea, menorrhagia, and the menopause are dealt with very fully, and the methods of treatment are well described.

The book, as we have said, makes a most welcome addition to the literature of this subject, and is characterized by the great care which has been shown in its production. There is a fine bibliography, though from an English point of view it is discouraging to see that practically no reference is made to English publications on the subject. Almost without exception the papers referred to are of American or Continental origin.

Review of Current Literature.

Director: FREDERICK ROQUES, M.A., M.D., M.Chir. (Cantab.), F.R.C.S., F.R.C.O.G.

THIS Review contains the lists of contents and abstracts of the more important articles from the following journals with which the "Journal of Obstetrics and Gynaecology of the British Empire" exchanges:—

British.—The Lancet; British Medical Journal.

Canadian.—The Canadian Medical Association Journal; Bulletin Médical de Quebec.

Australian.—Medical Journal of Australia; The Australian and New Zealand Journal of Surgery.

Indian.—The Calcutta Medical Journal.

American.—American Journal of Obstetrics and Gynecology; The Journal of the American Medical Association; Surgery, Gynecology and Obstetrics; American Journal of Diseases of Children.

French.—La Gynécologie; Gynécologie et Obstétrique; Bulletin de la Société d'Obstétrique et de Gynécologie de Paris.

Belgian.—Brûxelles Médical.

Italian.—Annali di Obstetrica e Ginecologia; Archivo di Obstetrica e Ginecologia; Revista Italiana di Ginecologia, Bologna.

German.—Archiv für Gynäkologie; Zeitschrift für Geburtshülfe und Gynäkologie; Zentralblatt für Gynäkologie; Monatsschrift für Geburtshülfe und Gynäkologie; Münchener Medizinische Wochenschrift; Monatsschrift für Krebsbekampfung.

Scandinavian.—Acta Obstetrica Scandinavica.

South American.—Boletin de la Sociedad Obstetrica y Ginecologia de Buenos Aires.

Japanese.—Japanese Journal of Obstetrics and Gynaecology.

The Review of Current Literature thus keeps the readers of the Journal in touch with current literature throughout the world. At the end of the year an Index of all the subjects contained in the articles of the above journals is printed. Arrangements are also made to include abstracts of important articles on border-line subjects, such as Physiology, Biology, and Biochemistry.

LIST OF ABSTRACTORS

London: J. BEATTIE, F.R.C.S.; A. C. BELL, F.R.C.S.; R. K. BOWES, F.R.C.S.; J. LYLE CAMERON, F.R.C.S.; ALBERT DAVIS, F.R.C.S.; F. H. FINLAISON, F.R.C.S.; B. GILBERT, F.R.C.S.; R. J. KELLAR, F.R.C.S.; R. LIGHTWOOD, F.R.C.P.; J. A. MOORE, F.R.C.S.; C. D. READ, F.R.C.S. (Edin.); F. ROQUES, F.R.C.S.; R. WINTERTON, F.R.C.S.

Felsted: W. E. CROWTHER, M.B.

Leeds: R. H. B. ADAMSON, M.D., AND B. JEAFFRESON, F.R.C.S.

Liverpool: M. DATNOW, F.R.C.S.; P. MALPAS, F.R.C.S.; T. N A JEFFCOATE, F.R.C.S.

Manchester: R. NEWTON, M.D.

Glasgow: JANE H. FILSHILL.

The Canadian Medical Association Journal.

Vol. xl, No. 4, April, 1939.

*Chorion-epithelioma following ectopic gestation. W. A. Dafoe.

CHORION-EPITHELIOMA FOLLOWING ECTOPIC GESTATION.

The author reviews reports indicating the frequency with which chorion-epithelioma follows hydatidiform mole, giving quotations from case reports of various authors. The incidence varied between one and 44 per cent and is believed to be somewhere in the region of 10 per cent.

It is admitted that the growth may occur after full-time pregnancy, after abortion, in teratoma of the testes and from other indeterminate causes. Histological appearances do not seem to afford any indication of the degree of malignancy of the growth, the prognosis being still unpredictable. Estimations of gonadotropic hormone in the urine are of great value as confirmatory evidence and in the diagnosis of this type of growth, although it must be borne in mind that a negative test does not ensure entire absence of the neoplasm.

Thomas, in 1934, reports a case of ectopic gestation followed by chorion-epithelioma. He also reviewed the literature on the subject up to this date which revealed that the number of reported cases was 35.

The author reports two cases of chorion-epithelioma following first, interstitial ectopic gestation, and secondly an ampullary implanation of the pregnancy. In the first case the uterus and right adnexa were removed, chorion-epithelioma was found in the interstitial portion of the Fallopian tube, metastases occurred in the lungs as verified by examination six weeks later; the patient died in three and a half months. The growth had invaded all the surrounding structures locally in the pelvis, and almost all the abdominal viscera were also involved.

In the second case a tumour filling the right side of the pelvis and appearing to spring from the tube was discovered and removed, together with the Fallopian tube. After operation the patient developed fluid in the chest. Three weeks after operation she expelled a normal decidual cast of the uterus. A secondary mass appeared in the vagina some weeks later, and microscopic section showed this to be chorion-epithelioma. Two weeks later the mass had shrunk to a small size. Six milligrams of radium were applied for five days to the affected area. An Aschheim-Zondek test, which was positive before the application of the radium, became negative afterwards. A month later the affected area was healed, although a small mass was felt to the right of the uterus. Examinations made twice during the following year revealed that the mass in the pelvis had completely disappeared. The patient was alive and well five years later.

The histological appearances of the tumours in both cases were identical.

A short bibliography is appended.

J. LYLE CAMERON.

The Journal of the American Medical Association

Vol. cxii, No. 6, February 11th, 1939.

Pelvic type and its relation to body-build in white women. William Greulich and Herbert Thoms.

*Testosterone propionate in the treatment of functional uterine bleeding. H. S. Rubinstein.

Vol. cxii, No. 7, February 18th, 1939.

*The management of tuberculosis of the cervix uteri. D. C. Collins.

Ruptured ectopic pregnancy: a helpful diagnostic sign. L. Brady.

Vol. cxii, No. 9, March 4th, 1939.

Experimental eclampsia. Editorial.

Vol. cxii, No. 11, March 18th, 1939.

Pneumococcal pneumonia complicating pregnancy and the puerperium. M. Finland and T. B. Dublin.

Vol. cxii, No. 14, April 8th, 1939.

Contraceptive methods. I. S. Stein.

Vol. cxii, No. 16, April 22nd, 1939.

Maternal mortality in Cleveland. R. A. Bolt.

Foetal death. Edith L. Potter and F. L. Adair.

Circulation in pregnancy. M. E. Cohen and K. J. Thomson.

Vol. cxii, No. 18, May 6th, 1939.

Parovarian cysts complicating pregnancy. Wendell Downing and Lawrence O'Toole.

Sterile motile spermatozoa. Frances I. Seymour.

Testosterone Propionate in the Treatment of Functional Uterine Bleeding.

The patient described was aged 35 and had suffered from excessive menstrual loss for about 10 years. She was stout and sexually frigid, but had had five pregnancies; clinical tests indicated the presence of hypopituitarism with secondary hypothyroidism. The endometrium was of the non-secretory type. The patient was first treated with thyroid extract and a low calorific diet, but this had no effect on the bleeding, which lasted 10 to 12 days with almost continuous staining in the intervals. Testosterone propionate, in doses of 5 milligrams, was at first administered twice weekly, and the periods were at once reduced to five days at 28-day intervals, with no intermenstrual staining. The dose was reduced to four injections of 5 milligrams each during the intermenstruum, and the menses have remained normal.

REVIEW OF CURRENT LITERATURE

THE MANAGEMENT OF TUBERCULOSIS OF THE CERVIX UTERI.

Six new cases are here reported to add to the list of known instances of this rare condition. The disease should be differentiated especially from carcinoma, biopsy being the method of choice. The author strongly advocates radical surgical treatment when this is not contra-indicated by extensive local spread to local viscera, marked secondary infection, the presence of active tuberculous foci elsewhere, cardiovascular disease and senility.

A brief review is made on the literature on the subject.

F. H. FINLAISON.

Surgery, Gynecology and Obstetrics

Vol. lxviii, No. 4, April, 1939.

*Excision of the superior hypogastric plexus (presacral nerve) for primary dysmenorrhoea. J. V. Meigs.

*A consideration of certain types of benign tumours of the placenta. A. A. Marchetti.

*Arrhenoblastoma. M. B. Dockerty and W. C. McCarty.

*Tubal resection as a treatment for recurrent gonorrhoeal salpingitis. H. C. Falk.

*Intraperitoneal haemorrhage from ruptured ovarian retention cysts; corpus luteum and Graafian follicle cysts. F. J. Harris and M. J. Groper.

Hydatidiform mole and chorion-epithelioma. Editorial.

EXCISION OF THE SUPERIOR HYPOGASTRIC PLEXUS (PRESACRAL NERVE) FOR PRIMARY DYSMENORRHOEA.

Resection of the superior hypogastric plexus or presacral nerve reduces uterine spasm and vasoconstriction. A patient with uterine dysmenorrhoea referred to the region of the anus and coccyx, and not into the lumbar or ovarian region, should obtain relief by this operation, but a patient with a questionable type of dysmenorrhoea, will probably obtain no relief.

In a considerable number of cases this operation was found to change the patient's menstrual habits. Backache does not appear to be controlled by the superior hypogastric plexus. Meigs thinks that this operation which appears formidable, is the best treatment for patients with true primary dysmenorrhoea.

A CONSIDERATION OF CERTAIN TYPES OF BENIGN TUMOURS OF THE PLACENTA.

Benign tumours of the placenta designated as chorio-angiomata, are relatively rare. These tumours are differentiated into several types; the cellular or immature, the vascular or more mature type and that type accompanied by varying degrees of degenerative changes are presented. These

forms may intermingle in all gradations in the same tumour. The histogenesis of these tumours is fairly well established. The tissue originates from the chorionic mesenchyme, the proliferating endothelium and blood-vessels playing the leading role, the stroma a subordinate or accessory role. Whether the neoplasm is a true tumour according to Ribbert's idea or a malformation as explained by R. Meyer is still an open question. Clinically, it is believed that chorio-angiomata are of little significance.

Arrhenoblastoma.

Dockerty and MacCarty present in this paper four cases of arrhenoblastoma. The clinical syndrome of sterility with amenorrhoea, hirsutism, atrophy of the breasts, hypertrophy of the clitoris and changes in the voice, were all noted in two cases. In one case absence of follicular hormone with an increase of anterior pituitary hormone was found on examination of the urine.

These tumours are of a low grade of malignancy and in most instances respond well to surgical removal. All four cases are reported here in detail.

Tubal Resection as a Treatment for Recurrent Gonorrhoeal Salpingitis.

Cornual resection of the Fallopian tubes is here offered as a surgical procedure for the cure of recurrent gonorrhoeal salpingitis. The technique is as follows.

The abdomen is opened by a left paramedian incision from the symphysis to the umbilicus. After insertion of the self-retaining retractor, three laparotomy pads are placed so as to pack away the omentum and intestines. The adhesions of omentum and small intestines to the pelvic organs are severed by blunt or sharp dissection. The fundus of the uterus is identified and the adnexa inspected. The condition of the ovaries is the deciding factor for the type of operation to be performed. If an ovarian abscess or cyst is found salpingo-oöphorectomy is performed; if no ovarian disease is found a resection of the tube can be carried out. A figure of 8 stitch is inserted in the uterine horn proximal to an artery clamp placed on the uterine end of the tube. A V-shaped excision of the uterine end of the tube is made so as not to injure the underlying ovarian branch of the uterine artery. The proximal end of the tube is freed from its mesosalpinx by cutting the mesosalpinx close to the tube for a distance of one centimetre. The figure of 8 suture in the uterus is tied, left long and a clamp applied. A ligature is applied to the cut end of the tube and the clamp removed. The long end of this suture is threaded on a needle which is passed through the posterior wall of the uterus below the ligament of the ovary and tied. This automatically causes the cut end of the tube to be inverted under the tube itself. The same procedure is carried out on the other side.

In 112 cases there was no primary mortality and no primary pelvic morbidity; 70 per cent were perfect, 14 per cent good and 7 per cent fair anatomical results. There were no re-operations for pelvic disease and no re-admissions for recurrent salpingitis.

INTRAPERITONEAL HAEMORRHAGE FROM RUPTURED OVARIAN RETENTION CYSTS.

The authors have reviewed a series of 45 patients with ruptured ovarian retention cysts, and the study of this group of cases shows remarkable variations in the pathology, clinical diagnostic features and aetiology. A classification into three groups of mild, moderate and massive haemorrhage resulting from rupture of ovarian retention cysts is described. The clinical aspects of this entity are determined by the amount of intraperitoneal bleeding. The diagnosis of the condition is dependent upon time relation to the previous menstruation, characteristic variation in abdominal pain and tenderness, the presence of active peristalsis and frequently positive pelvic findings. Rupture of an ovarian retention cyst must be differentiated from acute appendicitis, ectopic pregnancy, pelvic inflammatory disease and torsion of the pedicle of an ovarian cyst.

The majority of these cases can be treated by conservative observation. The tendency to recurrent attacks is rare but if it does occur, the possibility of endocrine therapy.

If surgical intervention proves necessary, a plastic resection of the cyst, with preservation of normal ovarian tissue is advocated.

C. D. READ.

La Gynécologie

Vol. xxxviii, January, 1938.

*A case of dystocia caused by the scar of lower segment Caesarean section. R. Fournier.

Excision of the vagina as the operation of choice in genital prolapse occurring in old women. J.-R. Pinsan.

Lighting up of infection of the Fallopian tubes. J.-R. Pinsan.

Various complications of toxaemia occurring in a patient with severe cardiac disease. P. Muller.

*Subcapsular haematoma of the liver occurring in a newborn child followed by intraperitoneal haemorrhage. P. Claer.

Some remarks on early hysterectomies and the removal of fibroid tumours by the Strasbourg surgeon Koerberlé. P. Meyer.

Vol. xxxviii, February, 1939.

*The present state of prognosis in malignant epithelial and primitive tumours of the ovary. Jacques Mathieu.

*Remarks on cancer of the ampulla of the Fallopian tube. Charles Ambre.

Vol. xxxviii, March, 1939.

*The treatment of vaginismus due to persistence of the hymen. Louis Funck-Brentano and Paul Funck-Brentano.

Lower segment Caesarean section and low insertion of the placenta. L. Digonnet.

The diagnosis of tumour plus pregnancy near term. J. Courtois.

Report of the International Congress at Amsterdam, 4th and 8th May, 1938.

An abnormality in the lower segment of the uterus following lower segment Caesarean section. J. Courtois.

A Case of Dystocia Caused by Scar of Lower Segment Caesarean Section.

The writer describes a case in which, following a previous lower segment Caesarean section, the head was arrested by a fibrous band in the situation of the old operation scar. He postulates that in all lower segment Caesarean sections the upper part of the uterine wound is much thicker than the lower. Adequate suture is therefore impossible, and there is a predisposition to form an imperfect fibrous scar.

Subcapsular Haematoma of the Liver in a Newborn Child.

The author points out that these cases are infrequent, only about 30 reports having been published since 1936. In the case described the patient had had three previous children with normal labours in each confinement. The Wassermann test was strongly positive. With her fourth child she had a normal labour; the child cried immediately after birth and there were no signs of asphyxia. The child, however, was pale and jaundiced. This latter feature increased during the second and third days, but the child took the breast quite well. On the morning of the fourth day the child quite suddenly became very ill and white and died a few minutes later.

Post-mortem revealed that the peritoneal cavity was flooded with blood, some of this being coagulated. There was a large subcapsular haematoma of the liver. This was on the surface of the organ near the right lobe and the capsule was perforated.

The author thinks that the cause of the haemorrhage was an abnormal fragility of the veins, probably due to the syphilitic condition of the mother.

Prognosis in Malignant Epithelial and Primitive Tumours.

This author points out that the question of prognosis in these tumours is open to discussion. In his paper he limits himself to the common epithelial type of tumour and treats the question largely from a clinical standpoint.

The clinical picture is often misleading in these cases. Even the rapid development of a large abdominal tumour does not necessarily indicate malignancy. The symptoms are often vague and indecisive. Emaciation and

general bodily ill-health are often discovered apart from malignancy. The age incidence is again unreliable. He stresses that in the vast majority of cases it is impossible to make a definite diagnosis of malignancy before operation.

The operative findings are much more important. The following features must be noted as they are all of importance from the standpoint of prognosis. The presence of ascites has no special significance, and even blood-stained ascitic fluid is not conclusive of malignancy.

Bilateral tumours occur both in benign and malignant types. The author points out that although a tumour may be apparently unilateral, the other ovary may be the site of histological change. The general appearance of the tumour is important. Large solid irregular tumours, cavitated and containing necrotic material are usually malignant. On the other hand simple tumours with only small papillary projections perhaps, on their internal aspect, are usually benign, but there are exceptions to these also. Occasionally extensions of the tumour are found on the peritoneum, the omentum, and even adhering to the intestine, when the surface of the tumour appears smooth and regular.

The author mentions the cases collected by Taylor and Alsop, published in 1932. In all these cases peritoneal deposits disappeared after removal of the ovaries. These cases were verified during subsequent laparotomy. They believe therefore that secondaries in the pelvis or in the intestine are not necessarily indicative of malignancy, but it is very difficult to differentiate from the non-malignant variety. They point out that the appearance at operation alone can never afford sufficient evidence for certain prognosis

Histological studies of the various tumours have been made by the author. Five cases which exhibited all the classical signs of advanced malignancy are mentioned and all these patients lived a long time after the operation. Others, on the other hand, when there was little or no mytosis or atypical cells, and when one was inclined to give a good prognosis, the patients died in a very short time.

Any prognosis based on the histological picture in this solid type of tumour is far from exact. In the cystic type of tumour much more value may be laid on the histological picture. The ordinary tumours with papillary projections do not present so insoluble a problem. Any prognosis based on their histology has for a long time been thought valueless. Recently, however, the work of Taylor seems to show that a careful cytological examination can prove of great assistance on this question of prognosis, and the work of the present author confirms the affirmations of Taylor. The author has given a classification of ovarian tumours based upon their origin from the germinal epithelium or from Wollfian relics. He points out that such a classification is by no means purely academic, as the mere fact of being unable to diagnose the origin of the tumour elements with certainty gives rise to a suspicion of malignancy. Out of 85 cases the author has been unable to place the origin of the tumour 10 times, and out of these death followed rapidly in 7 cases. The following signs of a benign tumour are given: strict limitation of the tumour, atypical cellular types, and abnormal nuclei; absence of epidermal metaplasia, absence of stroma reaction and hyalinization, absence of necrosis.

If all these criteria of non-malignancy are present then there need be little doubt of one's prognosis. However, one must be more guarded if the tumour is of Wollfian origin than if it arises from the germinal epithelium. Infiltration of the stroma is an almost certain indication of malignancy, and this holds for the Wollfian tumours as well as for those from the germinal epithelium. The presence or absence of inflammatory reaction seems to be of small prognostic import. The presence of zones of necrosis is a sign of malignancy upon which stress has been insufficiently laid. The heaping up and metaplasia of the epithelium of the tumour is, of course, a valuable sign.

Basing the prognosis on all these signs the author has been able to give a reasonably exact prognosis in all but 15 per cent of his cases. Occasionally, of course, cancerous change supervenes on a benign but proliferative type of tumour.

When dealing with solid tumours evidence gained at operation and by microscopy is notoriously unreliable, and in the prognosis of this type of tumour the author uses a different technique. This consists in basing the prognosis rather on the summation of the various signs and symptoms rather than paying too much attention to histology. Occasionally in this type of tumour abnormalities in the menses, feminization, masculinization, or a positive Aschheim-Zondek reaction may occur, and each of these affects the prognosis. Menstrual irregularities are rare in ovarian tumours, and one is often struck by the fact that the menstrual rhythm has been maintained in spite of massive infiltration of both ovaries by tumour. Sometimes excessive haemorrhage occurs. This phenomenon was noticed in 19 cases out of 119. The presence of haemorrhagic losses must always be noted. When these abnormal losses occurred a histological examination of the whole genital tract was made. Sometimes a tubal deposit was discovered, sometimes a metastatic nodule in the cervix or body of the uterus, sometimes a condition resembling adenomyoma, and in one case, in which the endometrium was examined it gave the appearance of having been treated by radium. However the presence of metastatic nodules cannot always be demonstrated by any means. Occasionally after the normal menopause ovarian tumours cause a reappearance of the menstrual flow. These tumours are of the granulosa type, and feminizing in character. The virilizing tumours of the ovary tend to occur between the ages of 21 and 35. In this type of patient amenorrhoea is the rule.

A further group of tumours is described from the viewpoint of prognosis—the seminomata and the chorion-epitheliomata.

Cancer of the Ampulla of the Fallopian Tube.

Until recently epithelioma of the Fallopian tube has been considered a rare disease. The author has searched in the laboratory at Lyons and has found 10 epitheliomata in this situation. He points out that the condition is not so rare as has been formerly supposed, and that every surgeon sees several cases. The histories of 7 cases of carcinoma of the Fallopian tube are recorded. The condition may occur in either Fallopian tube, probably more commonly

on the right side. In one of the cases collected by the author the lesion was bilateral. These tumours may differ very much macroscopically. They may simulate a hydrosalpinx, haematosalpinx, or an ovarian tumour. In three of the cases which were studied by the author dense adhesions to the rectum or parietal peritoneum existed; ascites was never present in any of these cases. If the appearance of the tumour when the abdomen was opened was indefinite, the true diagnosis was always obvious on opening the Fallopian tube. Most of the lesions occurred in the ampullary part of the tube. In each of the recorded cases the uterus was healthy apart from small seedling fibroids in one or two. In one case only was the ovary enveloped and surrounded by the tumour. Only rarely were typical histological types encountered in this series. Most of the growths were of the alveolar or papillary variety. Most of the patients were between 40 and 60 years of age, and the majority of them were over 50; and, contrary to the previously published statistics of Bair, Le Balle, and Pattay, only one patient was still having normal menstrual periods. Five of the patients had passed the menopause many years previously. Only one of the patients was known to have borne children, and four of the patients were nulliparae. None of these patients had had any fever during their illnesses; this is a very important point in the diagnosis, as in these cases one suspects inflammatory lesions of the adnexa. One patient had become very emaciated, but most of them presented no characteristic general sign. Pain was often described but varied in type. In two cases a watery discharge from the uterus occurred, and in two others a sanious discharge mixed with blood. In two cases the watery discharge was the only symptom of the disease. Only in three or four cases was the diagnosis made before operation. In three the tumour was diagnosed as uterine, and was thought to be a fibroid or a carcinoma of the uterine body. In three other cases the lesion was thought to be an inflammatory condition of the adnexa. The treatment in most cases was total hysterectomy; although in two patients the affected Fallopian tube was extirpated under the impression that the condition was not malignant. The author thinks that Wertheim's hysterectomy is unnecessary, and advocates pan-hysterectomy. Subtotal hysterectomy is dangerous because of the possibility of metastatic growth in the lower part of the uterus. Post-operative radiotherapy is probably an advantage, and the good results of several authors are collected. There is no place for radium in the treatment of this condition. As so few cases are on record the prognosis is still open to doubt, but it seems fairly certain that tumours in this situation are of a high degree of malignancy.

The Treatment of Vaginismus with Persistent Hymen.

This condition very often occurs in nervous, unstable women, and in many of these people the psychologist can do more to help the patient than the surgeon. Cases with a persistent hymeneal membrane must, of course, be surgically treated. The vaginal sphincter is very complicated anatomically, and arranged in three layers. The superficial layer includes a thin posterior muscle strip, the transverse superficial muscle, and also the bulbo-cavernosus muscle. This is a feeble sphincter. The intermediate layer is formed by the

deep transverse perineal muscle. The third and deepest layer is by far the most important, and is formed by the powerful sling of the pelvic muscles. The method of treating vaginismus described by the author is an attempt to mimic the dilatation and distension of the perineal muscles produced in childbirth. This dilatation is obtained with a Champetier de Ribes's bag. This is introduced empty and filled after its introduction into the vaginal canal. Traction is applied to the bag and a mock labour produced. This type of dilatation of the vaginal canal is gradual and the dilating agent has the advantage of being elastic. The condition is not always cured by such a dilatation, but then even normal childbirth cannot be guaranteed to cure vaginismus.

The second part of the treatment consists in excision of the hymen. It must be remembered that the hymen very often constitutes the irritative focus which has given rise to the vaginismus. It is better to excise the hymen completely, and a satisfactory approach to the membrane must be obtained. The author advises excision of the hymen with the Chapmetier de Ribes's bag in the vagina. Excision performed in this way is very simple because the membrane is stretched over the projecting part of the bag, and can be easily isolated and excised in a circular fashion.

General anaesthesia is recommended for the operation, cyclopropane being the ideal vehicle. The actual technique of excision of the hymen over the bag is described, and diagrams and pictures included.

C. E. B. RICHARDS.

Gynécologie et Obstétrique.

Vol. xxxix, No. 2, February, 1939.

An anatomical and therapeutic study of ovarian endometriosis. G. Cotte, J. Mathieu.

*The results of oöphorectomy in pregnancy. L. Verangot Portes.

Four lower segment Caesarean sections, with exclusion of the peritoneum Mikulicz drainage.

*The serum phosphatase in pregnancy. de Kerleau, J. Cayla.

*A study of abortifacients, apiol, rue, savin, mug wort. (1) Their action on non-pregnant animals. A. Patoir, G. Patoir, H. Bédrine.

The effect of bimanual crushing of the corpus luteum on menstruation. N. Kakuschkin.

Vol. xxxix, No. 3, March, 1939.

Strabismus and congenital syphilis. A. Fruhinsholz, J. Louyot.

*Two hundred and ninety-nine cases of the lower segment operation. L. Digonnet.

*The problem of the innervation of the uterus. J. Mahon.

Azotaemia in the normal puerperium. J. Chosson, P. Dor.

Two points in the technique of the lower segment operation. H. Ezes.

*A study of abortifacients, apiol, rue, savin, mug wort. (I) Their action on pregnant animals. A. Patoir, G. Patoir, H. Bédrine.

REVIEW OF CURRENT LITERATURE

The Results of Oöphorectomy in Pregnancy.

The authors have assembled various reports on the effect of removing the corpus luteum of pregnancy. In the rabbit, rat, mouse, goat, cow, the integrity of the corpus luteum is indispensable to the continuance of pregnancy. In the guinea-pig, cat, dog, mare, the corpus luteum can be removed at a very early stage without prejudicing the pregnancy. In man the evidence is not conclusive and they quote four cases from the literature in which bilateral oöphorectomy performed before the fortieth day of pregnancy was not followed by abortion.

The authors interpret this evidence as showing that other tissues besides the corpus luteum secrete progesterone.

The Serum Phosphatase in Pregnancy.

This paper, by Caderas de Kerleau and Cayla, records an investigation into the rôle of serum phosphatase in foetal ossification and follows the work of Robison.

During the first six months of pregnancy the serum phosphatase remains the same as in the non-pregnant women. In the third trimester of pregnancy the value rises considerably. The value rapidly falls to normal after delivery. The results show that the fixation by the foetus of the calcium and phosphorus it needs for the development of the skeleton is a phenomenon of later pregnancy.

The Action of Certain Abortifacients, Apiol, Rue, Savin, Mug Wort.

The authors have confirmed experimentally the view that the action of these abortifacients is an indirect one and that if abortion follows their use it is secondary to a maternal hepatitis and nephritis.

Two Hundred and Ninety-nine Cases of the Lower Segment Operation.

Digonnet records his personal cases. He has had 14 maternal deaths, a mortality of 4.68 per cent. Four of the deaths occurred in elective cases, of shock, haemorrhage, pulmonary embolism and broncho-pneumonia respectively. In the elective cases the morbidity was 14.9 per cent. In suspect cases there were 7 deaths, 2 from haemorrhage, 2 from peritonitis, 1 from ileus, 2 from general infections. The morbidity was 21.6 per cent. In infected cases there were 3 deaths, 9.09 per cent, 2 from septicaemia, 1 from general peritonitis. The morbidity in infected cases was 45.4 per cent.

The Innervation of the Uterus.

Mahon records his experimental findings of the actions of various drugs on the uterine contractions in parturient women. He confirmed that adrenalin, a sympathetic stimulant, is without action on the uterine contractions,

but does sometimes raise the uterine tone. Ergotamine tartrate, a sympathetic inhibitor, stimulates uterine contractions. Pilocarpine increases the power of the contractions in conformance with its known vagotonic action. Atropine, on the other hand, an inhibitor of the parasympathetic, definitely diminishes the contractions.

In general the author concludes that the central nervous system controls the intermittent contractions of the uterus, inhibiting the tone of the body and increasing the tone of the cervix. The parasympathetic is the accessory motor nerve of the uterus, controlling the intermittent contractions and the sympathetic is the nerve maintaining the uterine tonus.

AZOTAEMIA IN THE NORMAL PUERPERIUM.

The authors record their findings of the non-protein-nitrogen content of the blood following delivery. Their results show that the value falls at the time of labour, rising slightly thereafter to a maximum on the sixth day of puerperium. In none of the authors' experiments did the value rise above what are usually considered normal limits. The explanation of this puerperal rise may be twofold, a reduction of hydraemic plethora and the increased muscular metabolism following labour.

P. MALPAS.

Archiv für Gynäkologie.

Band clxviii, Heft 2, February 24th, 1939.

Porphyrin excretion in the urine in hyperemesis gravidarum and in eclamptic and pre-eclamptic conditions. H. Mittelstrass.

*The microscopical examination of material from puncture of the pouch of Douglas: its significance in the diagnosis of tumours. K. Schmidt.

*Pseudopregnancy, with a note concerning the interpretation of positive Zondek-Aschheim reactions in the absence of demonstrable pregnancy. H. Limburg.

The occurrence of fatty tissue in uterine tumours. H. Greve.

*The results of conducting labour, in breech presentations, in hospital. J. Erbslöh.

*The large ovary. E. Fauvet.

*The effect of combined administration of follicular hormone and testosterone propionate on the genital organs of castrated female rats. E. Steinkamm and H. Meckies.

The composition of the vernix caseosa. R. Schmid.

*The glycogen content of the vaginal epithelium in childhood and its modifications after the administration of follicular hormone. K. Herrnberger and F. H. Hortsmann.

REVIEW OF CURRENT LITERATURE

The excretion of oxytocic substances in the urine during pregnancy. K. Sievers, R. Neumayer and R. Depper.

*Carcinomatous metastases in the ovary, with special consideration of Krukenberg tumours. W. Uhlmann.

Preparatory treatment in gynaecological operations. H. Dietel.

*Hepatic function in normal pregnancy and hyperemesis gravidarum. L. Herold.

The effect of nicotine on fecundity in the female of Lebistes heticulatus. E. Schuster-Woldan.

*The influence of section of the hypophyseal pedicle on lactation. L. Herold.

The trichomonas problem and the occurrence of the parasites in human blood. W. Schultz and A. Westphal.

The Microscopical Examination of Material from Puncture of the Pouch of Douglas: Its Significance in the Diagnosis of Tumours.

In some 54 cases, without untoward results, the posterior fornix has been punctured and if necessary aspirated: the solid parts in the resulting material are embedded in paraffin and examined in sections. In all cases the antecedent diagnosis was doubtful. Four results were negative (no solid material); inflammatory disease was found in 26, and tumour in 12. In five cases normal fat resulted and two rectal mucosa was the only yield.

Pseudopregnancy, with a Note Concerning the Interpretation of Positive Zondek-Aschheim Reactions in the Absence of Demonstrable Pregnancy.

Pseudopregnancy, as has been known since Wagner's classical case, with functional endometrial hypertrophy, persisting corpus luteum and amenorrhoea may be due to hormonal disturbances of the antuitary. Cases in which laparotomy is not done or the endometrium has not been examined microscopically are to be regarded very critically. So far the literature has only mentioned two cases of corpus luteum persistens in which the Zondek-Aschheim reaction, if done, was positive. Limburg records the case of a woman aged 45 whose endometrium, after 8 days' uterine bleeding occurring 8 days after 14 days' bleeding which began a week after regular menstruation had been expected, was reported as an intact " decidua of pregnancy (functional hypertrophy) without chorionic elements ". Three weeks later the uterus and left adnexa were removed for submucous myoma: no trace of an ovum could be found. The right ovary, left *in situ*, contained a recently ruptured follicle: the left small follicular cysts and a large regressing corpus luteum with wide luteal layer. The Zondek-Aschheim reaction was strongly positive as late as 5 weeks after the curettage, probably from pathologically increased prolan excretion by the antuitary, which however radiologically showed no sign of tumour. The newly formed endometrium, in the extirpated uterus, showed, 3 weeks after curettage, a normal proliferation stage of the twelfth

and thirteenth day. In the laboratory concerned there were in 18 months five other cases in which the Zondek-Aschheim reaction was positive (grade III) although no signs of pregnancy could be found. These cases are described in detail: two, it is concluded, may have been examples of persisting corpus luteum.

THE RESULTS OF CONDUCTING LABOUR, IN BREECH PRESENTATION, IN HOSPITAL.

Some 400 cases from Danzig are analysed: those with an infant less than 44 cm. in length, or 1500 gm. in weight, are excluded. The maternal mortality was 0.9 per cent: the foetal mortality 9.8 uncorrected and 6.3 when corrected for prematurity and those dead on admission. To improve these results Erbslöh recommends the more conservative conduct of the labour which progresses smoothly, and the more frequent adoption of Caesarean section in elderly primigravidae. The danger of asphyxia in breech delivery has been exaggerated, and that of injury to the skull under-estimated. Traction from below is to be replaced by pressure from above and medicinal stimulation of the uterine contractions; the Smellie grip should be used only when the head is completely within the pelvis; dystocia from the soft parts must be regarded more seriously, and an adequate episiotomy done in all primigravidae who have gone to term.

THE LARGE OVARY.

The term, as such, is stated to have been first applied in 1911 by Bartel and Hermann to abnormally voluminous ovaries found in the presence of constitutional anomalies: their series appears to have included both (1) large solid ovaries and (2) large ovaries containing numerous small cysts. Fauvet now describes six cases of large ovary. They comprise respectively (1) solid, functionally insufficient ovaries, with excess of loose connective tissue and a paucity of germinal plasma: (2) solid enlargement due to secondary scarring accompanying excessive rate of follicular growth and regression; here also the organ was functionally insufficient: (3) large cystic ovaries in a young subject, the expression of increased, certainly not diminished, function, of pituitary causation: (4) a similar finding in an eclamptic: (5) two cases in which enlargement was due to oedema of the stroma and pseudocystic distension of regressing follicles from stasis accompanying paraovarian cyst. The variety of ovary described under the third heading is now frequently seen in Germany during operations for eugenic sterilization.

THE EFFECT OF THE COMBINED ADMINISTRATION OF FOLLICULAR HORMONE AND TESTOSTERONE PROPIONATE ON THE GENITAL ORGANS OF CASTRATED FEMALE RATS.

References are given to experimental work in human and animal subjects which seems to point to a suppression of the cyclical uterovaginal changes when testicular hormone is added to follicular hormone. The present paper

confirms Korenchewsky's finding (*Biochem. Journ.*, xxxi, 780, 1937) that the combined administration of the two is followed by a growth of the vaginal epithelium in which the superficial layer is composed of cylindrical cells showing evidence of secretion. This however does not appear to be mucus. A similar finding was noted in the lower part of the cervix. The epithelial changes are likened to those noted during pregnancy.

THE GLYCOGEN CONTENT OF THE VAGINAL EPITHELIUM IN CHILDHOOD AND ITS MODIFICATIONS AFTER THE ADMINISTRATION OF FOLLICULAR HORMONE.

Daily doses of 1000 international benzoate units, or more, of oestradiol benzoate given by the mouth to children led to a well-marked accumulation of glycogen in the vaginal epithelial cells, as shown in smear preparations. The preparations were stained by Best's method after being at once fixed in absolute alcohol. The richness in glycogen of these cells in the newborn is confirmed: it is absent or scanty from 6 months to 12 years, and present in considerable amounts before and at puberty.

CARCINOMATOUS METASTASES IN THE OVARY, WITH SPECIAL CONSIDERATION OF KRUKENBERG TUMOURS.

Uhlmann analyses 40 specimens of metastic ovarian carcinoma: of these 22 had the well-known Krukenberg characteristics and 11 might possibly be included in the same category, although mucus formation was absent. Among the 22, 15 were metastases of a primary tumour in the alimentary tract, and in 6 no autopsy was made. There remained one case in which the primary nature of a Krukenberg tumour seemed certain. Details of a further recent similar case are appended. It seemed clear that in at least one-third of cases metastases occurred from implantation.

HEPATIC FUNCTION IN NORMAL PREGNANCY AND HYPEREMESIS GRAVIDARUM.

The signs which are well known to denote danger in hyperemesis, notably icterus and cerebral symptoms, may appear too late for termination of pregnancy to save life: hence the value of early objective signs of hepatic functional impairment, recognizable by biochemical tests. These tests however must be carefully correlated with the clinical findings. Herold details the results of the following tests, done in each of a series of 25 patients with severe toxic hyperemesis gravidarum. Carbohydrate metabolism was tested by the alimentary galactosuria test; protein metabolism by Ambard's serum-urea estimations and by those of the serum-xanthoprotein values; bile pigment metabolism by measuring the serum-bilirubin; and metabolism of the porphyrin bodies by estimation of urinary porphyrins by Schreus's and Carrié's spectrocolorimetric method. The chief features noted were (1) increase of urinary galactose and delayed reduction of the blood-sugar after feeding, (2) increase of non-protein nitrogen, blood-urea and xanthoprotein titre, and,

probably more important, delayed diminution of free and delayed increase of combined amino-nitrogen after the intravenous injection of amino-acids, (3) increase of serum-bilirubin, frequently with positive direct van den Bergh test, (4) increase of porphyrinuria, independently of increased erythrolysis. On the whole greater importance is to be attached to the results of the consumption tests. No reliable guide in considering induction is afforded by any one test alone of partial hepatic function; a consideration of two tests, however, both pointing to impairment, is of very considerable weight. Herold regards as the most significant (1) a combination of positive xanthoprotein reaction, increase of blood-bilirubin and positive galactose feeding test, (2) signs of defective hepatic de-aminizing function, i.e. increase of free and combined amino-nitrogen during fasting, as well as finding, after the administration of protein or protein components, of delayed fall of free and delayed rise of combined amino-nitrogen in the blood, and of absence of the characteristic rise in blood-urea which in normal pregnancy begins after 60 minutes, (3) increased urinary porphyrin.

INFLUENCE OF SECTION OF THE HYPOPHYSEAL PEDICLE ON LACTATION.

The expulsion of the placenta leads to sudden diminution in the corpus luteum hormone in the body, and thus to an outpouring of the lactation hormone from the antuitary. Herold here reports that section of the hypophyseal pedicle in lactating rats led within a few days to cessation of lactation: he concludes that a peripheral nervous stimulation, that of suction by the infant, is necessary for the maintenance of milk production. Lactation, brought about entirely by hormones, cannot be maintained in the absence of reflex nervous impulses travelling through the hypophyseal pedicle.

W. E. CROWTHER.

Zentralblatt für Gynäkologie.

No. 11, March 18, 1939.

*The pathogenesis of extra-amniotic pregnancy. H. Meyer-Rüegg.
The treatment of primary uterine inertia with folliculin. M. Nagel and H. Bachmann.
Euflamin in the treatment of adnexal inflammatory disease. H. Montag.
An operation for senile prolapse after Kahr. F. C. van Tongeren.
The results of the subtotal colpokleisis after Labhardt. P. Feldweg.
The value of the disappearance of blood copuscular sinking in gynaecology. K. Mauks.
Fertility after Caesarean section. H. Tüscher.
The treatment of anal fistulae, fissures and periproctitis with short-wave diathemy. W. Baumgarts.

No. 12, March 25, 1939.

Simultaneous measurement of the spinal distance and the true conjugate diameter by radiology. K. Kimmig.

Findings with polarographic examination of the serum from women with genital carcinoma. R. K. Kelkel.

Chemotherapy of gonorrhoea in the female. W. Pfister.

Myasthenia gravidarum. A. V. Fekete.

The raising of the power of lactation with the aid of the electric breast pump. W. Schweizer.

No. 13, April 1, 1939.

Obituary of E. Sontag. P. Diepgen.

Death from acute heart block in eclampsia without convulsions. P. Ottow.

Probable intra-uterine death from heart block in the foetus. Confirmed clinically in the newborn. B. Ottow.

Follicular hormone substitute (Cyren-Bayer) and its influence on the arrest of lactation and influence on lactation. W. Lindemann.

The pathological picture in cervico-vaginal fistula. O. Bauer.

The aetiology of congenital wry neck. H. Kastendieck.

Observation on the article "Menstrual bleeding and trauma," by Professor Mayer. D. v. Raisz.

No. 14, April 8, 1939.

Abdominal actinomycosis with special reference to a case of genital actinomycosis in the female. A. Vonessen.

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THE PATHOGENESIS OF EXTRA-AMNIOTIC PREGNANCY.

Meyer-Rüegg refers further to the case of extra-amniotic pregnancy which he described in *Zentralblatt für Gynäkol.*, 1904, 51, H.3. The mother was a trained nurse who had assisted at many intra-uterine operations. When she became pregnant and all the usual abortifacient drugs had been unsuccessfully used she inserted a knitting needle through the cervix and punctured the membranes. There was a gush of clear watery fluid at the time and a leakage for a few days afterwards. There was no bleeding and no evacuation of the uterine contents. Pregnancy continued until the twenty-eighth week and then ended

in the birth of a premature dead foetus. The foetus, placenta and membranes were delivered in one mass with the previous loss of liquor amnii. The placenta and chorion formed a sac containing the foetus and the liquor amnii. The amnion was entirely stripped off the chorion and placenta up to the attachment of the cord and contained only the cord, the upper part of the abdomen, the chest in front and the face of the foetus to which it was adherent. The part of the foetus inside the small amniotic sac was grossly defective. The upper part of the abdominal wall was incomplete and there was a hernia of the liver into the left side of the chest and displacement of the heart to the right. The skull was defective with almost complete absence of the left half of the brain, a frontal meningocele, double hare lip and cleft palate were present.

The writer considers that in this case the amnion was torn in the early weeks of pregnancy, while the two membranes were separated by the remnants of the magna reticulare. The opening in the chorion again closed, but the tear in the amnion did not close. Deprived of its contained amiotic fluid the delicate amion came in contact with the upper part of the foetus and adhered to it, causing great deformity. He considers that all extra-amniotic pregnancies start as intra-amniotic with rupture of the amnion in the early weeks of pregnancy. Though he has found records of only 12 cases he thinks that the condition is more common than this would suggest.

He further refers to the case of a woman whose first pregnancy had been terminated, and at the attempt to evacuate the second one at the sixth week introduction of the curette led to such severe bleeding that it was feared the uterus had been perforated. The operation was stopped and packing introduced. He does not state whether the uterus or the vagina was packed. The patient recovered and the pregnancy was uninterrupted. The foetus was born at full time and survived with the following deformities: amputation of the right leg below the knee, and amputation of the left little finger and left great toe. The writer thinks that though a tearing off of these parts by the curette cannot be excluded yet that it is more likely that shreads of the amnion were torn off and became adherent to the parts which were later constricted and amputated.

Myoma, Sterility and Fertility.

Huber discusses the connexion between the existence of myomata and sterility. Up to the present he does not consider that the cause of the sterility has been established. Whether the myoma is the cause of the sterility, or whether the sterility is the primary condition followed by the growth and development of the myoma, or whether they are both a sign of some controlling hormonal or constitutional disturbance is uncertain. Pregnancy in a myomatous uterus is by no means rare. If myomata was the cause of sterility then one would find a greater frequency of sterility with large tumours and a lesser frequency with small ones. In actual practice this is not found to be the case.

During operations upon patients suffering from myomata one often finds

sufficient other changes in the pelvis which would be an adequate cause of sterility. Further, as Schumacher pointed out, the age of women beginning with primary and secondary sterility compared with that when treatment for myoma is called for is so long—14 to 16 years—that it seems certain that the sterility may have existed before the beginning of the myoma. In the case of beginning myomatous change sterility already begins to be noticed long before the size of the tumour can have any mechanical effect.

On histological examination of 162 interstitial portions of the Fallopian tubes in myomatous uteri, the writer found tubal endometriosis in 89 cases and patent tubes in 73 cases—54 per cent. He found that this condition was far more frequent in the case of multiple myomata than in the solitary myoma. The 89 cases of endometriosis were divided into 67 multiple and 22 single myomata. The 73 free cases were divided into 29 multiple and 44 single myomata. That is to say, out of 66 cases of solitary myoma there were 22 cases of endometriosis, i.e. 33.3 per cent., and out of 96 multiple myomata there were 67 cases, i.e. 69.6 per cent. In 29 per cent of cases of endometriosis both Fallopian tubes were completely occluded; in the rest, the occlusion was not absolute in both tubes.

In treating a sterile patient with myomata certain points should therefore be considered. A certain number of cases of pelvic endometriosis have had a previous myomectomy performed. In his own 22 cases 4 had previously had myomectomy performed. Myomectomy for sterility is not to be recommended except in cases in which the Fallopian tubes are known to be patent.

Essential Anomaly of the Fatty Tissues in the Whole Body of a Newborn Foetus.

Szolnoki reports the case of a foetus suffering from a curious condition. The mother had been treated during this, her fifth, pregnancy for a urinary infection with pyrexia, and at the time of delivery the urine contained a cloud of albumin. The foetal heart stopped three minutes after delivery, and there was no attempt at respiration. The whole surface of the skin was smooth and stretched; the whole surface was desquamating. Apart from being slightly microcephalic the foetus was normally developed. The limbs were stiff and the fingers and toes spread wide apart. On post-mortem examination the foetus was found to be covered by a thick layer of fat, 1 to 2 cm. thick. This fatty hypertrophy of the subcutaneous layer was complicated by a high grade keratosis and, in some places, calcification.

Severe Intra-Abdominal Bleeding from a Myoma in the Eighth Month of Pregnancy.

Wolfring records a case of severe intra-abdominal bleeding from a ruptured vein over a myoma. Laparotomy was performed for an acute abdominal catastrophe which was thought to be due to acute appendicitis. On opening the abdomen, which was full of blood, the size of the pregnant uterus was such

that the bleeding point could not be found. As the patient was *in extremis* it was decided to remove the uterine tumour by Caesarean section and subsequent subtotal hysterectomy. The patient recovered after a blood-transfusion. The foetus was stillborn. Examination of the operation specimen showed a ruptured vein over a uterine myoma.

The writer points out this is the first case of such a haemorrhage that he has heard of occurring in pregnancy, and the first record of intra-abdominal bleeding from a myoma since the 13 cases reported by Benzel in 1917.

Microcephaly in the Newborn.

Klöppner refers to the small weight of the brain in microcephaly. The smallest weight recorded was one of 15.9 grams in a boy aged 7 years, and 283 grams in a woman of 43 years. The normal weight of the brain in an adult man is 1,360 grams, and in an adult woman 1,220 grams; in newborn males it is 400 grams, and in newborn females 380 grams.

True microcephaly must be distinguished from pseudo microcephaly. The first results from a developmental defect in the brain and the second from accidental processes which damage the brain such as inflammatory changes or haemorrhages. The true microcephalic brain shows primitive convolutions and sulci; the spinal cord is narrowed due to contraction or absence of the pyramidal tracts. The theories of the causation of the condition's being atavistic, as in the so-called ape man (C. Vogt), or due to the early closure of the cranial sutures (Virchow), are not now held. At the present time the condition is thought to result from toxic damage with, perhaps, some mechanical or thermal injury to the reproductive cell. For instance, Gatti describes cases with severe alcoholism in the father.

It is not considered that all cases result from damage to the sperm, as severe cases have resulted from radiation of the ovum in the early weeks of pregnancy. In recent times there have been several cases of microcephalic children after radiation, so that A. Mayer deliberately carried out a therapeutic abortion in a patient who was found to be pregnant after a course of radiation for irregular bleeding. Goldbladt pointed out that microcephaly may be a familial defect as in the case of the B family in Bürgel. Here the father had three normal children by his first wife, and by his second nine children, of whom five were microcephalic. Bernstein recorded a family of 10 of whom five were high-grade microcephalics and mental defectives. Pilcz recorded a family of five microcephalics and six hydrocephalics. Ellsworth found in two families of hereditary microcephaly that on the mother's side there were other mental defects; he suggested that in these cases the mother's reproductive cells might have been responsible for the defects.

The writer further records three cases of microcephaly which occurred in the Obstetric Clinic at Tübingen, giving their clinical histories and post-mortem findings. The first baby survived its birth for five hours; it also had a double cleft palate and hare lip. Post-mortem examination showed the meninges to contain fluid and only a very small brain, most probably representing the mid brain. The second baby survived for 20 days. Apart from the

very small head and enormous ears there were no other malformations. During its life an entire investigation of its nervous reflexes was carried out. This foetus appeared to be blind and deaf and to have no sense of smell. There was some suggestion of the sense of taste to salt and bitter flavours. There was some degree of spastic paresis. Post-mortem examination showed an entire absence of the cerebrum and cerebellum, leaving only the medulla oblongata, mid brain and basal ganglia. The third baby died at home at 54 days from difficulties in feeding. This child had a typical bird face, and reminded one of the Aztec type. It had a great deal of lanugo covering the back, shoulders and upper arms. Neurological examination showed a great central and reflex excitability.

From the point of view of the obstetrician, the writer states that the second case was diagnosed radiologically after a clinical impression that the head was very small. In the third case the condition might have been suspected from the violent foetal movements which occurred with any uterine contraction.

A Teratoma of the Ovary with a Positive Zondek-Aschheim Reaction (Chorion-epithelioma of Teratomatous Origin).

Sbarcea reports from the University Clinic at Freiburg the case of a patient aged 27 years who was sent into hospital as a case of pregnancy for delivery. The patient denied the possibility of pregnancy at any time, but admitted having amenorrhoea for nine months; a tumour was found rising out of the pelvis, it was as large as the pregnant uterus at the twenty-eighth week. On vaginal examination the tumour could be defined as being related to the uterus, which was separated from it. An X-ray examination was made without any satisfactory result. The Aschheim-Zondek reaction was strongly positive, and on the strength of these investigations a diagnosis of malignant disease with early pregnancy was made.

Although the patient was very anaemic and pyrexial, laparotomy was performed. At the operation the uterus was found to be very small. A tumour was found on the left side, lying below the stretched out Fallopian tube, which was removed with the tube under the diagnosis of extra-uterine pregnancy. The patient survived the operation but died of metastases nine weeks later.

Examination of the tumour showed it to be a chorion-epithelioma. It was not clear whether this tumour was a primary growth in chorionic tissue in a teratoma or whether it was a chorion-epithelioma in a preceding ovarian pregnancy. The Aschheim-Zondek reaction remained strongly positive from the time of the operation until death. Before death there were secondary growths in the liver, lungs, brain and spleen, which accounted for the persistently positive reaction.

A Case of Embryonic Teratoma of the Ovary.

Bauer describes the case of a patient of 43 years who suffered from a teratoma of the ovary. The writer points out that of the 137 cases previously reported the greater number occurred in patients between the ages of 15 and

35 years. In only 7 cases was such a tumour found in a patient more than 40 years of age.

The writer's patient had had subtotal hysterectomy performed two years previously for a large submucous myoma; at that time the ovaries appeared healthy and were left in position. At her second operation a tumour the size of a foetal head was found arising from the right ovary; this was strongly adherent to all surrounding parts. The tumour was removed and the patient made an uninterrupted recovery; on subsequent examinations the patient remained well and showed no signs of any recurrence.

The histological examination of the tumour showed it to be a teratoma containing skin, cartilage, bone, muscle and nervous tissue.

R. H. B. ADAMSON.

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*The theory and therapy of uterine inertia. H. Winkler and H. Vetter.

*The diminution of labour pains by means of rectidon. H. Gercke.

A collection of tubal pregnancies from the clinic. P. W. Logwinsky.

Remarks on the question of operative sterilization of women. K. Ehrhardt.

*Biological and X-ray demonstration of metastases in a case of chorion-epithelioma. E. Stockl.

*The clinical result of a large adnexal tumour treated surgically. O. Wolf.

*The value of basal metabolism for the clinic and pathology of eclampsism and eclampsia. F. P. Chanina and J. M. Burutschenkowa.

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The value of colposcopy in the investigation of malignant disease. H. Rogge.

*The question of a movable head above the brim of a primigravida. J. Farkas.

The interstitial form of tubal pregnancy. P. N. Logwinsky.

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An improvement of the operative technique of cranioplasty. E. Kehrer.

*The principles of fluor therapy. R. T. v. Jaschke.

*The action of anti-thyroid substances on the secretion of milk. P. H. Schumacher.

A communication on the question of toxic myocardial injury (narcosis á la reine and pre-eclampsia). H. Winkler.

*The potassium and calcium ratio in the gravid uterus; its value for uterine growth. H. Winkler.

*Disturbances following removal of one of the ovaries. H. Runge.
A case of complete inversion of the uterus. E. Wolfe.
*Myoma or extra-uterine pregnancy? L. Konigshoefer.
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*Pregnancy in essential hypertonia. H. Albrecht.
A lues reaction from the capillary blood developed for the purposes of consultation and advice concerning pregnancy. H. Schwalm.
A case of coccygeal teratoma successfully operated upon. K. Fuge.
*The clinical course of pregnancy anaemia and haematosis. M. A. Daniachi.

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Sterilization by means of X-rays for eugenic purposes. H. Naujoks.
*Fermentation inhibiting substances in the blood. The inhibiting substances in the blood of normal people, in toxicosis of pregnancy, and in uterine carcinoma. H. Eufinger and Sprado.
A communication on the pathology of intra-uterine fractures. K. Koch.
*Intra-uterine death as a result of ligature of the cord by torn amnion. H. v. Brucke.
A case of primary abdominal pregnancy with implantation on the spleen. W. Nagel.
The lymph during gestation and its relation to eclamptic fits. Fresel.
The calcium-potassium ratio in the pregnant uterus (two communications); its value for the tone of the uterine musculature and the reaction of the pregnant organism to calcium injections. H. Winkler.
The action of pregnancy urine on the germination of corn seeds. M. Bak.
*Regeneration of uterine mucosa after artificial abortion; hysteroscopic studies. B. Litwak and E. Wiktorowskaja.
Marked polyuria in a case of spina bifida occulta complicated by retroflexion and retroversion of the uterus. W. M. Chmelewsky.
The relation between the weight and the length of the newborn infant. W. A. Borissowa.

THE THEORY AND THERAPY OF UTERINE INERTIA.

The authors refer to work done by other investigators concerning the relation of electrolytes to contractions of plain muscle. Potassium and sodium are the most important, being antagonistic to each other. The potassium-calcium ratio is more important than an investigation of each substance separately.

The variation between the normal ratio and that of early and late pregnancy is discussed and illustrated. Intravenous injections of potassium lactate, chloride or phosphate in cases of uterine inertia produce no improvement. Investigations of the potassium rise and fall in the blood and its excretion in the urine following intravenous injection pointed the way to prove that the kidneys rapidly excreted potassium so that no action could be obtained.

Next, a series of investigations was commenced with a combination of calcium and quinine, which appeared to have some effect towards improving or bringing on labour pains. Altogether 101 cases were treated with the quinine calcium compound. A summary of the results is given.

THE DIMINUTION OF LABOUR PAINS BY MEANS OF RECTIDON.

The author describes his experiences in labour with rectidon, which is a preparation of barbituric acid. At first he gave 7 and later 8 c.c. of a 10 per cent solution with a maximum of 15 ccs. for every 10 kilogrammes of body weight, 5 kilogrammes being deducted for the pregnancy. More than 10 c.c. are never given now.

The solution is diluted with an equal part of warm water, and is introduced as high up into the bowel as possible, the bowels being first of all well cleared out by lavage.

The rectidon is given to the primigravida when the cervix is about the size of a five-shilling piece, and in multiparae when it is as large as a two-shilling piece. The effect commences roughly about a quarter of an hour after the injection and lasts for six to eight hours.

Thirty-seven multiparae and 68 primigravidae who have had the treatment all reacted in a similar manner. There is no influence on respiration or labour and no effect on the bowel or kidney. Sixty-one of the mothers were very pleased with the result; 12 others hardly remembered labour at all; 42 were not so satisfied. This is attributed to under-dosage. Only one patient was delivered operatively, owing to weakening of the pains. All the children were normal, one died two months after delivery. In 10 cases the liquor was stained with meconium.

BIOLOGICAL AND X-RAY DEMONSTRATION OF METASTASES IN A CASE OF CHORION-EPITHELIOMA.

The author describes in great detail a case in which the Zondek-Aschheim test was positive 57 days after combined radium and X-ray treatment of a chorion-epithelioma malignum. This led to a bad prognosis being given. Further investigation demonstrated the presence of metastases in the lungs. In spite of much X-ray and radium treatment, curettage still showed the presence of tumour cells and the patient finally died.

THE CLINICAL RESULT OF A LARGE ADNEXAL TUMOUR TREATED SURGICALLY.

The author analyses a series of 275 cases which were operated on for inflammatory adnexal tumours. He divides them into three groups:

1. Those with a diffuse associated peritonitis rather of an acute nature. There were 56 of these cases.

2. Those cases with a long history with repeated rises of temperature. There is gradual depreciation of the patient's general condition. There were 75 such cases.

The remaining 145 were patients who came because of symptoms attributable to adhesions, or to collection of fluids in the Fallopian tubes or ovaries.

Tables are given analysing the different types of cases, the infecting organisms, the age incidence, methods of treatment and their results.

The Value of Basal Metabolism for the Clinic and Pathology of Eclampsism and Eclampsia.

The author investigated 61 cases of pre-eclampsia and 47 cases of eclampsia, a total of 560 analyses was made. A table is given showing the amount of oedema, albumin and the height of the blood-pressure in groups of cases. Chemical investigations were carried out on the blood of the pre-eclamptics with reference to the nitrogen, calcium, potassium, sugar, reserve alkali, uric acid and ferments.

Tables are given to show the variation of these.

No parallelism could be demonstrated between the clinical severity of the cases and the chemical changes. Sugar showed no change from the normal.

There appeared to be a definite alteration in the calcium content in the cases of eclampsia. The blood-sugar also varied somewhat.

The alkali reserve was diminished. The uric acid was greatly increased. glycaemia was sometimes noticed, but its degree had no connexion with the severity of the condition.

Calcium and potassium salts appeared to be in normal quantities.

The Question of a Movable Head above the Brim of a Primigravida.

The author investigated a series of cases in which the head was movable above the brim at the beginning of labour. This is not always a sign of disproportion.

In 87 per cent of the cases spontaneous delivery occurred, in 66 per cent delivery was complete within 24 hours. The condition of the abdominal wall and the strength of the contractions play the most important role. He does, however, stress the fact that it is best to have these patients in an institution.

The Principles of Fluor Therapy.

The author points out that the cause of increased vaginal secretion may be either: (1) Increased permeability following mechanical or toxic injury to the epithelial cells so that secretion passes from the peri-vaginal connective tissues into the lumen. (2) The increased secretion may be due to the increased

permeability of the capillaries of submucosa and peri-vaginal vascular tissue. (3) There might be ionic disturbances originally dependant upon endocrine variations.

The author makes a theoretical discussion of all the constitutional causes that have been described as possible factors in bringing about fluor, amongst which he includes psychogenic factors. He states that although the trichomonas has been shown to be pathological in animals, he is not sure that it alone would cause vaginitis in human beings. He refers to the work of Bender who demonstrated three varieties of trichomonas, viz., buccalis, intestinalis and vaginalis. The author does not feel that the trauma which results from coitus is a causal factor of fluor.

Finally, he discusses vaginal flora, the acidity of the vagina and the glycogen content of the cells, none of which point to any form of treatment.

THE ACTION OF ANTITHYROID SUBSTANCES ON THE SECRETION OF MILK.

The author refers to the work of Kustner, and showed that restricted function of the thyreoid gland led to increased milk secretion. He found that by giving 2 tablets of thyronormal 3 times a day, and 1 tablet of di-iodo-thyroxin from the first day of the puerperium, the milk appeared sooner than in untreated cases. The total quantity of milk secreted in a day was also raised. Treatment during pregnancy made it possible for patients, who had not previously been able to, to feed their children.

THE POTASSIUM AND CALCIUM RATIO IN THE GRAVID UTERUS; ITS VALUE FOR UTERINE GROWTH.

The potassium content of the pregnant uterus increases from the beginning of pregnancy until its end, becoming about two and a half times the normal. The increase is highest in the last months of pregnancy. In the first months it remains constant. The quotient curve runs parallel with the calcium curve. The potassium and calcium values in pregnancy are similar to what were found by Guthman in gynaecological carcinoma.

DISTURBANCES FOLLOWING REMOVAL OF ONE OF THE OVARIES.

The author considers that removal of one appendage leads to typical disturbances. He gave a table showing the effect of extirpation of one ovary on the periods. In 52 per cent it was normal as before. In 13 per cent there was an improvement. In 4 per cent there was no change. In 7 per cent it was more frequent. In 2 per cent less frequent. In 9 per cent the loss was less, and in 5 per cent there was greater loss, in 3 per cent amenorrhoea.

MYOMA OR EXTRA-UTERINE PREGNANCY.

The author illustrates a case in which it was difficult to decide clinically whether an intra-uterine or extra-uterine pregnancy existed in association with fibroids.

PREGNANCY IN ESSENTIAL HYPERTONIA.

The author gives the clinical details in 5 cases of essential hypertonia, and shows that the prognosis is made grave in essential hypertonia because of the disturbance of the vasomotor tone regulation.

The physiological increase in tone of the sympathetic and parasympathetic systems with alteration of metabolism with an increase of the waste products of protein metabolism, throws much extra work on the vascular system and increases the risk of damage to the capillaries. The possibility of nephritic oedema and eclampsia therefore develops. In each succeeding pregnancy the signs become worse, and all cases of essential hypertonia should be considered grave from the beginning.

THE CLINICAL COURSE OF PREGNANCY ANAEMIA AND HAEMATOSIS.

The author describes six cases of severe anaemia in pregnancy. He illustrates the blood-picture and gives tables of the blood-counts.

FERMENTATION INHIBITING SUBSTANCES IN THE BLOOD. THE INHIBITING SUBSTANCES IN THE BLOOD OF NORMAL PEOPLE, IN TOXICOSIS OF PREGNANCY AND IN UTERINE CARCINOMA.

The invariable presence of fermentation inhibiting substances in the circulating blood, in healthy women during pregnancy and the premenstruum, and its absence from the blood of men and from that of women after the climacteric, suggests its dependence on ovarian function.

The authors made further investigations during pregnancy in patients suffering from carcinoma, and give a series of tables showing their results. With advancing pregnancy this inhibiting substance appeared in the blood and increased parallel with the growth of the foetus, disappearing again during the puerperium. An excessively high concentration of this substance is found in nephropathy and eclampsia. It does not pass through the placenta.

In cases of carcinoma the substance appears in the blood and increases considerably following radium and X-ray treatment.

INTRA-UTERINE DEATH AS A RESULT OF LIGATURE OF THE CORD BY TORN AMNION.

The author describes and illustrates the umbilical cord of a foetus which was ligatured in two places following premature rupture of the membranes.

REGENERATION OF UTERINE MUCOSA AFTER ARTIFICIAL ABORTION.

The author carried out a series of hysteroscopic examinations of the uterine cavity following abortion.

He found that it was possible to observe the regeneration of the mucosa. Five days after abortion it is also possible to find a good deal of epitheliazation, and after 9 days the epithelium is almost completely formed. Between the 18th and 21st days it is impossible to distinguish the uterine mucosa from the normal.

The regeneration occurs slowly from the tissues of the unchanged basal layer, from the glands, also from the reticulo-endothelial and adventitial cells of the interstitial tissues. In the first two days there is a good deal of lymphocytic infiltration.

M. DATNOW.

REPORTS OF SOCIETIES

THE NORTH OF ENGLAND OBSTETRICAL SOCIETY.

A meeting of the North of England Obstetrical and Gynaecological Society was held in Sheffield on March 10th, 1939.

A discussion on

A.R.P. IN RELATION TO MATERNITY WORK

was introduced by the President, Professor Farquhar Murray (Newcastle).

PROFESSOR FARQUHAR MURRAY based his remarks on the problems that would arise in the evacuation and treatment of obstetrical cases in the area served by the Princess Mary Maternity Hospital in Newcastle. In general he considered that whilst the ordinary routines would certainly have to be modified in an emergency, the decision to allow a patient to be sent home would have to be based on reasonably medical grounds and provisions made for future services. On two occasions at an interval of six weeks, he had made a test evacuation of the hospital, noting which cases could be sent home, what form of transport would be necessary, either ambulance or private cars, and whether the patient was to be discharged to the hospital district or to an outside area.

The two tests gave very similar results. Averaging the two it was found that of 82 cases in hospital, 69 could be evacuated and 13 would have to be left in hospital. These latter comprised cases of cardiac disease, toxaemia, puerperal infections, Caesarean section. Normal cases were sent home 24 hours after delivery. About half the cases could be sent home by cars, the others by ambulances.

He had consulted with the medical officers of health of the various areas concerned and had learned that they would accept responsibility for seeing that booked cases which could not be admitted because of the emergency would be cared for in their own homes by the county midwifery services.

As regards the hospital's own district, it would be necessary to provide transport and equipment for the extra confinements and nursing undertaken on the district, which could of course be larger than the hospital's normal district area. A removal of the whole hospital and its services to any new area would be unsound, as it would be unreasonable to expect women to follow the hospital and leave their families just because they were pregnant. His main contention was that a diffusion both of patients and of the necessary hospital services would be necessary.

Dr. Arthur Gemmell (Liverpool) thanked the President for his paper. He suggested that the two desiderata of keeping gravid women with their families and at the same time providing hospital facilities for them could be obtained by the registration of pregnancy, the interchange of information between local authorities allocating school groups of children and their parents to definite places in the reception areas, setting aside existing hospitals or houses in these areas as Maternity Units and by the allocation of extra obstetrical personnel to these areas. He thought some arrangements would have to be made for maternity beds and district midwifery in the dangerous areas.

Dr. Thierenz, Medical Officer of Health for Blackburn, suggested that the larger maternity units now in existence should be moved to existing or improvised outer-zone maternity hospitals, affiliated to one another. The affiliated bodies in each region would be administered by one central co-ordinating body responsible for the distribution of staff, patients and equipment. In the Blackburn area he had estimated that in a case of emergency about 6 per cent of births would still require admission to hospital. Dr. Thierenz opposed the scattering of midwifery services into numerous small and separated units.

Mr. A. Gough (Leeds) thought it likely that under times of strain the administration of a midwifery service would be difficult. He was strongly in favour of the evacuation of pregnant women from the danger zones, the provision of multiple small homes with some larger homes offering a more complete obstetrical service.

Professor Dougal (Manchester) considered the problem would have to be solved by the appointment of a Regional Obstetrical Officer with complete control of personnel and equipment.

The paper was also discussed by Dr. Stallybrass (Liverpool) and Mr. J. E. Stacey (Sheffield).

Professor MILES H. PHILLIPS (Sheffield) described

A NOTEWORTHY CASE OF BILATERAL SIMPLE PAPILLOMATOUS OVARIAN CYSTS.

The patient concerned, a nullipara, was 52 years of age. Her own doctor had found a large abdominal swelling in which he could palpate two distinct masses. The patient stated that the abdomen had been too large for several years, but that it had been increasing rapidly for a few months. She added that she had undergone an operation for the removal of an abdominal tumour 12 years ago, and that the abdomen had been too large ever since. This she had thought a consequence of such an operation or merely middle-age spread.

However, her friends told another story, in her absence. At the operation the surgeon had found an ovarian tumour which he had considered malignant. He had decided it was useless to attempt its removal and he had closed the abdomen, expecting her to die within a few months. No portion of the tumour was removed for microscopical examination. This gloomy prognosis and

even the fact that nothing had been removed was withheld from the patient, but she was advised to retire from her profession of teaching and, indeed, she had been in receipt of a disability pension ever since. She lived with, and kept house for a friend, a village schoolmistress. Her former doctor, now far distant, had been amazed to watch her continue to live, but another operation or opinion had never been suggested. He stated, in a letter, that " a papillomatous growth arising from the broad ligament had been found, but the surgeon had considered it too dangerous to attempt its removal." The surgeon himself, on inquiry, recollected the case and stated that " as it was probably malignant and obviously could not be removed without rupture and spread of the contents " he had thought it wiser to refrain from making the attempt. He added, on learning that she was still alive, " it now seems certain that it cannot have been carcinoma and very likely if I had got it out piecemeal, it being papillomatous, she would not now be alive."

Professor Phillips found a short, spare woman, not undernourished and not cachectic, with an enormous abdomen, larger than that of pregnancy at term. Two distinct large ovoid masses could be made out bulging the the abdomen and the flanks. No free fluid was detected.

On rectal examination a soft elastic swelling filling the true pelvis could be felt, but there was none of the frozen snow crackling sensation which is so suggestive of malignant papillary pelvic growths.

Menstruation had ceased two years previously. The bladder and bowels were functioning normally.

In view of these findings an exploratory abdominal operation was strongly urged, but several days elapsed and much discussion took place before the relatives would agree to this.

The operation was done under rectal paraldehyde and open ether. A very long incision was found necessary. There were only a few ounces of free fluid. It was quite impossible to dislodge intact either of the multilocular masses which bulged deeply into the flanks. Several papillomatous masses protruded from each of them, but there were no adhesions of any moment. The cyst on the right side was tapped, several pints of fluid being drawn off. The base of this cyst was then peeled out of the broad ligament, as easily as peeling a perfectly ripe orange. The ureter, quite normal in appearance, was thus exposed for several inches. In the hope of removing the left cyst intact, the body of the uterus, much flattened by pressure, was removed by Howard Kelly's technique, from right to left. However, it had such a broad pedicle and extended so deeply into the left loin that it also had to be tapped. In all 17 pints of fluid were collected. The operation was actually an easy one. The vermiform appendix, sharply kinked and swollen in its distal half, was removed. The patient made the most easy recovery. It was thought kinder, even wiser, not to tell her the whole story, for fear she might deplore the wasted years.

Each multilocular cyst, with a large loculus collapsed, was approximately 7½ inches in diameter. Most of the loculi were lined by cauliflower papillomatous processes; one of the cysts showed an extensive spread of these to the surface, the other only a small surface spread. Dr. Florence Scott Kirk,

Pathologist to the Jessop Hospital, has kindly examined several sections from each cyst and she reports that they are of a simple serous papillomatous nature. They are lined by a single layer of innocent-looking columnar epithelium. The connective tissue cores are for the most part hard and hyaline; a few areas show a more active epithelium and a more cellular stroma, but nothing indicates malignancy.

On looking through the literature for similar experiences, Professor Phillips found that Dr. C. J. Cullingworth, in the discussion on a paper by Alban Doran at the London Obstetrical Society in 1892, referred to two cases in which he had removed a papillary ovarian cyst at a second operation six and nine months respectively after an exploratory abdominal section in which he had released 15 and 17 pints respectively of ascitic fluid, but had feared to remove the proliferating and adherent masses of growth. Eighteen and 16 months respectively after the second operations each patient was in splendid health. Twelve years after this discussion, in the Ingleby Lecture of 1904, Cullingworth in "A Plea for Exploration in Suspected Malignant Disease of the Ovary," again referred to these two cases. The first patient had lived for 10 years and had then died from intestinal obstruction.

In Cullingworth's second case, in 1891, there had been bilateral cysts; he had removed only the left one, as the other was "collapsed and adherent." But seven years later he was inspired to re-open the abdomen and he then succeeded in removing a large adherent right cyst. She was still alive and well in 1904, six years later.

An equally apposite reference is to be found in Dr. Herbert Spencer's notable "Review of 658 Ovariotomies," an analysis of every one of his own cases, hospital and private, recorded in the Proceedings of the Royal Society of Medicine, May, 1933. Therein he states, "I am of opinion that the high frequency of malignancy in ovarian tumours stated in important treatises, viz. 20 to 25 per cent, is exaggerated and that the error is due to mistaking benign for malignant papilloma and fibroma for sarcoma." He adds, "I have personally removed 11 papillomatous ovarian tumours which had been declared after coeliotomy to be inoperable and, mostly, malignant, by experienced gynaecologists, of whom, I hasten to say, I was one. In only one of these cases did the tumours show definite microscopic evidence of malignancy, and in that case the patient survived the removal of the tumour for four years."

In his analysis of 50 cases of papillomatous cyst, 17 of which were malignant, Spencer records one case of bilateral cysts, with intra-cystic and extra-cystic papillary growths, in which at a previous exploratory operation by an experienced gynaecologist, only a small piece had been excised, for section, and pronounced malignant. Spencer removed both tumours as completely as seemed possible, but four years later he had to re-open the abdomen to excise a mass of papilloma off the broad ligament, and she was in good health 16 years later.

Professor Phillips said he could not refrain from repeating a characteristic comment made by Spencer, surely the most reliable of recorders. In analysing the fatalities in his whole series, and many of them were quite beyond human control, he tells of one patient who died "from peritonitis on the sixth day

after operation, from adhesion to gauze inadvertently left in the abdomen (but removed on the third day)." He adds, " with this sad case which affected me more than all the successful ones, I close my review."

With regard to the remarkable disappearance of diffuse peritoneal papillary implants after removal of the originating cyst or cysts, of which most of us have had experience, he referred those particularly interested to an article in *The American Journal of Cancer* on " Spontaneous Retrogression of Peritoneal Implantations from Ovarian Papillary Cystadenomata." An abstract of this is to be found in *The Journal of Obstetrics and Gynaecology of the British Empire*, Vol. xl, 682. Five new cases are recorded and 31 collected from the literature.

Professor Phillips ended with a significant quotation from Herbert Spencer's review. He lays down the " opinion based on experience that all benign ovarian tumours, however adherent or whether papillomatous or not, can and should be removed. Some of the benign and papillomatous tumours closely resemble malignant growths; if a patient, with such a tumour, is found two years after an exploratory operation to be fairly well, believe with me that you have made a mistake, and remove the tumour."

Dr. H. BURTON (Manchester) described

THE RESULTS OF SPINAL ANALGESIA IN LABOUR.

The technique employed was simple. A fine spinal needle of the Pitkin type was used. Many agents were tried before heavy percaine, 1/200, was decided upon. This agent gives an analgesic effect for at least 5 hours. Nine minims of the solution were used.

The patient sat up in bed with the spine arched as much as possible. The spinal needle was then introduced as usual between the fourth and fifth lumbar spines. The percaine was then introduced into the theca and the patient was kept in the sitting position for 15 minutes.

There were several precautions to be observed:

1. The patient should be kept absolutely even on the bed, with her buttocks level until the anasthetic is fixed. One tests this by asking the patient whether she feels pins and needles in the toes of both feet, and altering the position accordingly.

2. There has been a certain proportion of headaches subsequent to the spinal anaesthetic. This headache rarely occurs before the third day.

Various methods have been tried to overcome this difficulty. One method was the withdrawal of 40 drops of fluid before the anaesthetic is put in. The method which has served best, however, is one which was tried in the later cases on the suggestion of Dr. Ashworth. This is the so-called extra-dural tap, which is supposed to equalize the pressure inside and outside the theca and so stop leakage of cerebrospinal fluid.

The anaesthetic has been reserved for cases which have entered the second stage and its effect is thus estimated on the pains of this stage only. The

pains of the first stage can be admirably controlled by morphia. No sedative, however, has been given in these cases in order that the results may not be distorted.

Clinically it was observed that within 15 minutes of the anaesthetic's being given, the pains become appreciably less. The excessive abdominal pain was no longer felt and the patient was left with only a dull aching pain in the back. Involuntary bearing down disappeared.

An area of anaesthesia developed, the so-called saddleback area, which covers the perineum and anus. The muscles of the vulval outlet and the levator ani muscles were paralysed. This rendered the perineum extremely distensible.

Labour was prolonged, but with no ill effect on the child because of the absence of pressure on the head. The mother's condition became markedly relieved owing to the absence of bearing down pain. The mother was free from pain to such an extent that she had to be told when to bear down. This was done by a nurse who kept her hand gently upon the patient's abdomen and instructed her to bear down with each contraction. A moderate amount of fundal pressure might sometimes be found necessary.

In most cases the child is born normally and painlessly one to two hours after the injection. If no progress appears to be made it is easy to deliver the child's head with the forceps, no further anaesthetic being required. It is also noteworthy that repairs subsequent to either normal delivery or forceps delivery are also painless. Lacerations, however, were very infrequent in their cases owing to the distensibility of the perineum and the gradual easing out of the head.

Sixty primiparae were given the injection; 50 delivered themselves normally, 10 required the help of low forceps.

Fourteen multiparae delivered themselves normally.

Cardiac cases deserved a special mention with regard to this method of anaesthesia.

The dangerous stage in these cases is obviously the second stage, with its involuntary bearing down. It is precisely this sensation which is relieved by the analgesic agent.

Six cases of severe cardiac disease were given the injection. Three of these were extremely distressed with dyspnoea and cyanosis before the anaesthetic was given. The effect of the anaesthetic was truly remarkable in these cases. Two delivered themselves normally with perfect ease. The others were delivered with the help of low forceps.

Dr. Burton concluded with the mention of two other points:

1. There was no effect upon the blood-pressure in any of the cases. This is due, of course, to the fact that the anaesthetic area is much below the sympathetic outflow which is chiefly in the thoracic region.

2. Normal occipito-anterior cases were used so far as possible in their series. He would not care to state whether the forward rotation of an occipito-posterior would be affected by the paralysis of the levators. This was a question for further investigation.

Mr. T. F. Todd said, " This is a preliminary communication on a subject upon which I have been working for some time, namely the possible field for, and utility of, spinal analgesia in labour, and I wish to discuss this problem more from the theoretical aspect. First and foremost comes the question, ' Is spinal anaesthesia a safe procedure? ' The literature contains many references to the danger of spinal anaesthetics in labour (*vide* J. P. Greenhill, *Journ. Amer. Med. Assn.*, 1934, cii, 28; and T. L. Montgomery, *Journ. Amer. Med. Assn.*, 1937, cviii, 1679). The latter goes so far as to say ' it is the consensus of enlightened medical opinion that spinal anaesthesia is a dangerous anaesthetic in obstetric practice.' There is a minority of enthusiastic advocates, such as S. A. Crosgrove, P. O. Hall, and W. J. Gleeson, *Anaesth. and Analg.*, 1937, xvi, 234, but the general impression one acquires on reading the literature is that in labour there is an increased danger from spinal anaesthesia; many go so far as to question the legitimacy of its use at all. Most of us will probably have seen at some time or another a case of sudden death under spinal anaesthesia and there is certainly a prejudice against its use in labour on this score, besides the fact that it is technically more difficult to induce in view of the marked lordosis. However, most reported deaths have been associated with relatively large doses of spinal anaesthetic given with a view to doing Caesarean section. In one of my hospitals several hundred spinal anaesthetics have been given in the past three years for forceps deliveries and perineal repairs, a low spinal being given and a relatively small dose being used. No catastrophe has occurred, neither has there been any cause for alarm in any case. The technique described by Dr. Burton is I think even safer, inasmuch as lesser doses have been employed, a heavy agent has been used and the patient has been seated for 15 minutes. I doubt very much whether any catastrophe is likely to occur with this technique.

" The next point I wish to discuss is the rationale of this technique. All those who have witnessed a spinal anaesthetic being administered for a case of acute intestinal obstruction must have been struck with the following sequence of events: first, the intense pain disappears almost immediately; second, subjective phenomena are complained of and anaesthesia develops; finally, paralysis ensues. The sequence is analgesia, anaesthesia, paralysis. H. S. Gasser and J. Erlanger, *Amer. Journ. Physiol.*, 1929, lxxxviii, 581, showed that there was a differential rate of involvement of nerve fibres by an anaesthetic agent depending upon the diameter of the nerve fibres, the small fibres being affected first. The fibres transmitting pain impulses are considered to be the finest fibres in the nerve roots, and next in size the fibres transmitting other sensations and largest the motor fibres. The anatomical and physiological facts are substantiated by the effects of anaesthesia and suggest the possibility of obtaining a selective effect upon the pain fibres only. Theoretically it should be possible to achieve a selective effect by giving a minimal amount of the anaesthetic agent. In the experiment carried out by Dr. Burton and myself it has been abundantly proved to our satisfaction that it is possible to get such a selective effect with a minimal degree of anaesthesia and no motor paralysis at all. Dr. Burton has described the effects of this technique in the second stage of labour. In the first stage of

labour the bulk of the pain is visceral, transmitted through the upper two lumbar roots, and a low spinal anaesthetic will not affect these roots. I have demonstrated on several occasions that it is possible to relieve all the visceral pain of the first stage of labour by means of an injection of heavy percaine into the thoracic region between D.8 and 9, the patient being seated. I have found that an analgesic effect can be obtained using as little as 0.4 c.c. of heavy percaine. Such a small dose should be free from any risk, but this technique is open to the very obvious criticism that it is extremely difficult to tap the theca in the thoracic region and, more important still, it is possible to damage the cord with the spinal needle. My purpose in doing these experimental injections was merely to prove to my own satisfaction that it was possible to obtain a selective effect as none of these cases showed any recognizable degree of anaesthesia.

"We are presenting this note in the hopes of stimulating an interest into this extremely absorbing subject. If it is possible, and I think I can claim to have proved it, to obtain a selective effect by using a weak solution of a spinal anaesthetic, it should be possible to develop a technique whereby with correct postural modifications, the whole of the nerve roots concerned in the transmission of labour pains could be affected, namely L.1 and 2 and S.2, 3 and 4. It should be possible to obtain an anaesthetic agent that will produce a much more lasting effect than our present ones, of which percaine is the best in this respect. I think that if our experiments are repeated by other members and our results are confirmed, the problem should be presented to the experimental physiologist and pharmacologist. Theoretically it should be possible to give a spinal injection at the beginning of labour for the woman to have a completely normal and pain-free confinement. I realize that this sounds too Utopian to be likely, but my own feeling is that the problems awaiting solution are all capable of being solved. There is no alternative method of analgesia in labour that gives us a conscious, co-operative and contented patient."

A meeting of the North of England Obstetrical and Gynaecological Society was held in Leeds on April 21st, 1939.

Mr. A. GOUGH (Leeds) described

A CASE OF CARCINOMA OF THE RECTUM AND PREGNANCY

The patient was a woman 30 years of age, who was 3½ months advanced in her second pregnancy. She sought advice on account of persistent diarrhoea of three months' duration. She was an exceptionally robust patient, full-blooded and well-nourished, but not at all obese.

On abdominal examination the uterus was found just rising out of the pelvis. By the rectum a hard, annular growth was felt at a distance of four inches from the anus.

It was decided to deal radically with the carcinoma, and leave the pregnancy to take its chance. A combined abdomino-perineal operation was undertaken and completed in one sitting. The abdomen was first opened through a left paramedian incision and the intestine was mobilized from the middle of the sigmoid down to the pelvic floor. This was decidedly difficult because the pregnant uterus took up so much room. It had to be held out of the way, and it was undoubtedly subject to a good deal of trauma. The laparotomy wound was completely closed.

The patient was then placed in an exaggerated lithotomy position. A median incision was made, starting an inch behind the anus and extending back three inches. The coccyx was freed and removed. The levator ani muscles were divided well away from the rectum. All the attachments of the intestine were progressively separated until a large loop hung out of the wound. The part removed extended from 8 inches above the growth to 2 inches below it. The anal canal was preserved and an end-to-end suture was done round a large rectal tube. The perineal wound was partly sutured, the rest being packed with chloramine gauze.

The histological examination showed a typical columnar-celled carcinoma. No malignant deposits were found in the glands.

The laparotomy wound healed by first intention; the perineal wound suppurated, but healed in 6 weeks. The pregnancy continued to term and the patient has just been delivered of a living child weighing 8½ pounds.

The operation performed in this case may be called ideal proctectomy, i.e. free removal of a considerable length of bowel containing the growth with conservation of a normally-situated and normally-functioning rectum. This is not often possible. It necessitates a case in which there is a fairly early growth not too near the anus, and in which the patient is in very good condition. A similar operation can be done in two stages with an interval of three or four days: this certainly reduces the risk, but gives less chance of a satisfactory union of the sutured intestine.

This adds one more to the long list of cases in which a pregnancy has continued undisturbed in spite of severe trauma to the pelvic organs. Some patients miscarry after such trivial causes as sneezing, whereas others will go to term after violence has been applied to the uterus itself.

The President congratulated Mr. Gough on his successful case. He had seen 2 women with colostomy openings become pregnant and continue to term without any derangement of the stomata.

Mr. A. GOUGH and Dr. LISSIMORE (Leeds) described

A CASE OF ENDOMETRIO-CARCINOMA OF THE UTERUS.

The patient was 57 years of age and she had 10 children.

During the past seven years there had been irregular bleeding from the uterus, alternating with a yellow discharge. She had had some vague pains in the lower abdomen and back. By a combined examination it was easy to recognize an enlargement of the uterus, which corresponded in size to a three months' pregnancy, although its consistence was much firmer.

A diagnosis of carcinoma of the body of the uterus was made. It will be realized that two features of the case-history cannot easily be squared with that diagnosis, namely the long duration of the haemorrhage, and the fact that the patient had had 10 children.

Panhysterectomy was performed, and the naked-eyed examination of the specimen appeared to confirm the diagnosis previously made. It was Dr. Lissimore's subsequent investigation which revealed the very interesting pathological condition which he left him to describe.

Dr. Lissimore discussed the question whether the endometriomatous change favoured the development of the carcinoma. He had encountered two similar cases previously in Leeds.

Dr. K. V. Bailey (Manchester) asked whether the ovaries had been examined for endometrial changes as in some cases of uterine endometrioma the ovaries were invaded.

Mr. Malpas (Liverpool) wondered whether the evolution of some cases of carcinoma corporis might not be much slower than is usually considered the case.

In reply Dr. Lissimore said he had found Schroeder's cystic hyperplasia in half the cases of carcinoma corporis he had examined. Mr. Gough said the ovaries were not examined microscopically because at the time of operation there seemed no doubt that the case was a straightforward one of cancer of the uterine body.

Mr. D. Currie (Leeds) showed

A SPECIMEN OF FALLOPIAN TUBES AND UTERUS REMOVED SOME YEARS AFTER CONSERVATIVE TREATMENT BY INJECTIONS OF PROTARGOL.

The patient, aged 39, had complained for a long time of backache, discharge and heavy periods; prior to admission into hospital she had suffered from an

acute attack of abdominal pain. Following an examination a diagnosis of tubal pyosalpinx with pelvic haematocele was made. This was proved to be correct, and the uterus and both Fallopian tubes and both ovaries were removed.

The interesting point was that seven years prior to operation she had complained of low abdominal pain. A diagnosis of salpingitis had been made and after the abdomen had been opened both tubes were injected with a solution of protargol, in the hope that the infection would settle down and the tubes remain patent, in order to allow for a pregnancy.

In the discussion Dr. Lissimore (Leeds) said he had found a tubal endometriosis in every case of ectopic gestation he had seen and he did not consider a decidual reaction occurred anywhere except in an endometrial stroma.

The President thought lipiodol is a better antiseptic to inject into the tubes than protargol.

Mr. D. Currie (Leeds) described)

A Case of Menopausal Haemorrhage Treated by Deep X-Rays.

The patient, aged 45, attended the Women's Hospital on 31st August, 1938, with a complaint of heavy periods. Her doctor's opinion was that she had menorrhagia of menopause and that an artificial menopause should be induced because of the severe losses she had experienced. The patient was fully aware of the various methods by which an artificial menopause can be produced and had decided upon deep X-ray therapy as the method for her case. She was very much averse from any operative interference. The uterus was slightly enlarged, hard and tender.

Arrangements were made for her to see the radiologist, but owing to the method of transfer of patients he did not see her until 14 days after her attendance at the hospital. By that time she was seven days past the expected date of her period and she made a comment to the radiologist about this, remarking that it was unusual and that she had never experienced a delay before. This fact did not impress the radiologist and a full menopausal dose of deep X-ray therapy was given at one application.

Later, in November, she saw the radiologist and reported the absence of periods and the presence of some morning sickness. In January, 1939, she had no doubt whatever that she was pregnant and was again referred to Mr. Currie by her doctor, who was worried about the outcome of the pregnancy following the application of deep X-rays. Mr. Currie ventured the opinion that since she could have been little more than 21 days pregnant when X-ray therapy was given, if damage had been done it should have led to an abortion, and that he could not picture the rays picking out any particular part of the embryonic plate in such an immature embryo.

The pregnancy progressed normally until the thirty-sixth week when it was noticed that the child's head was a little larger than was expected. At the thirty-eighth week an X-ray photograph revealed a large hydrocephalic head.

Labour was induced by puncture of the membranes and the stillette passed through the fontanelle, with the liberation of 16 oz. of cerebrospinal fluid. The head collapsed and a normal labour followed.

A majority of those present agreed that the proper course had been adopted in allowing the pregnancy to continue. Mrs. Adamson (Leeds) referred to the published German work which dealt with the incidence of malformations, particularly microcephaly, after irradition. The case was discussed by the President and Mr. Malpas.

In reply, Mr. Currie said he had recently begun to question the value of inducing the menopause with radium, and had found vaginal hysterectomy a more satisfactory procedure.

Mr. G. Blomfield (Leeds) described

A Case of Locked Twins.

Pregnancy was complicated by a toxaemia. Labour started prematurely at the thirty-fifth week. The first twin was quickly born as far as the umbilicus. It was necessary to disengage the head of the first twin from the head of the second forecoming vertex, whereupon extraction was easily effected. In the puerperium the patient developed an acute suppurative streptococcal arthritis of the right knee, which was treated by repeated aspiration of the pus, on Thomas's splint, and prontosil. The arthritis cleared spontaneously, and the only residual disability was a little stiffness. Both children survived.

Of 14,677 deliveries in Leeds there were 220 sets of twins. Among these twins there was a potentiality of locking in 30 cases, 26 with the first twin a breech and the second a vertex, 4 with the first twin a vertex and the second a breech.

The President thought the condition was favoured by a roomy pelvis and prematurity.

Mr. A. Gough thought impaction could occur with other varieties of twin presentation.

Mr. Jeaffreson (Leeds) described a case he had seen a week ago in which he had diagnosed locked twins because of a multiplicity of limbs in the pelvis. However, it proved to be a case of Siamese twins.

In his reply, Mr. Blomfield stressed the importance of distinguishing between locking and collision of twins.

Dr. K. V. Bailey (Manchester) showed

An Abdominal Retractor

which he had devised to overcome some of the disadvantages of the Doyen model for intrapelvic surgery. The instrument consisted of two flat blades hinged together at one end and controlled by a ratchet. When closed the two

blades lie in apposition so that introduction is easy, when fully opened the two blades lie at an angle of nearly 180°. The instrument possessed certain advantages over the rigid Doyen retractor. It was more readily introduced and therefore did not require such complete relaxation of the recti. The flat blades minimized the amount of trauma inflicted on the recti muscles. The fact that the two blades form an acute angle enabled the instrument to fit well down into the lower angle of the incision, thereby opening up the whole length of the incision for access to the pelvic organs. With an incision of six inches more than an extra inch of access was obtained as compared with a rigid retractor. The instrument had been made for Dr. Bailey by Messrs Thackeray of Leeds.